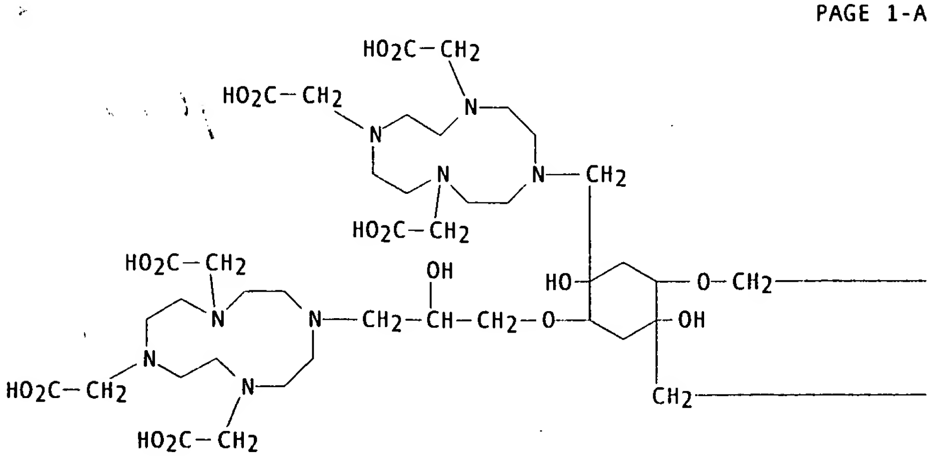
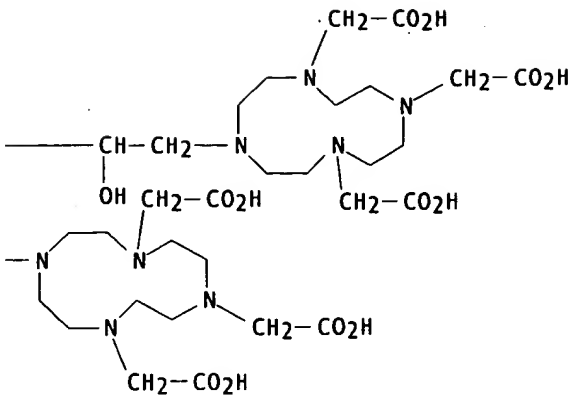
09/476022

```
=> screen 2076

L1     SCREEN CREATED

=>
Uploading c:\stnexp4\queries\29448289.str

L2       STRUCTURE UPLOADED

=> que L2 AND L1

L3   QUE L2 AND L1

=> s l3

SAMPLE SEARCH INITIATED 10:13:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     24 TO ITERATE

100.0% PROCESSED      24 ITERATIONS                              11 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE   **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:          187  TO      773
PROJECTED ANSWERS:              22  TO      418

L4            11 SEA SSS SAM L2 AND L1

=> d scan


L4   11 ANSWERS   REGISTRY  COPYRIGHT 2001 ACS
IN   1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[[2,5-
     dihydroxy-2,5-bis[2-hydroxy-3-[4,7,10-5-tris(carboxymethyl)-4,7,10-
     tetraazacyclododec-1-yl]propoxy]-1,4-cyclohexanediyl]bis(methylene)]bis-
     (9CI)
MF   C70 H124 N16 O30
CI   COM
```

PAGE 1-A





HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> s l3 sss ful

FULL SEARCH INITIATED 10:14:00 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 533 TO ITERATE

100.0% PROCESSED 533 ITERATIONS 308 ANSWERS
SEARCH TIME: 00.00.04

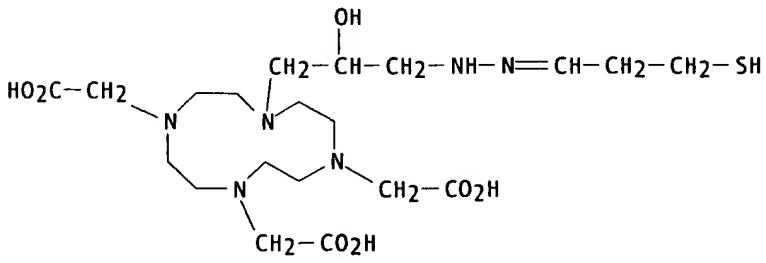
L5 308 SEA SSS FUL L2 AND L1

=> s l5 and nrs=1

5409679 NRS=1
L6 80 L5 AND NRS=1

=> d scan

L6 80 ANSWERS REGISTRY COPYRIGHT 2001 ACS
IN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(3-mercaptopropylidene)hydrazino]propyl]- (9CI)
MF C20 H38 N6 O7 S



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> s l5 and nrs=2

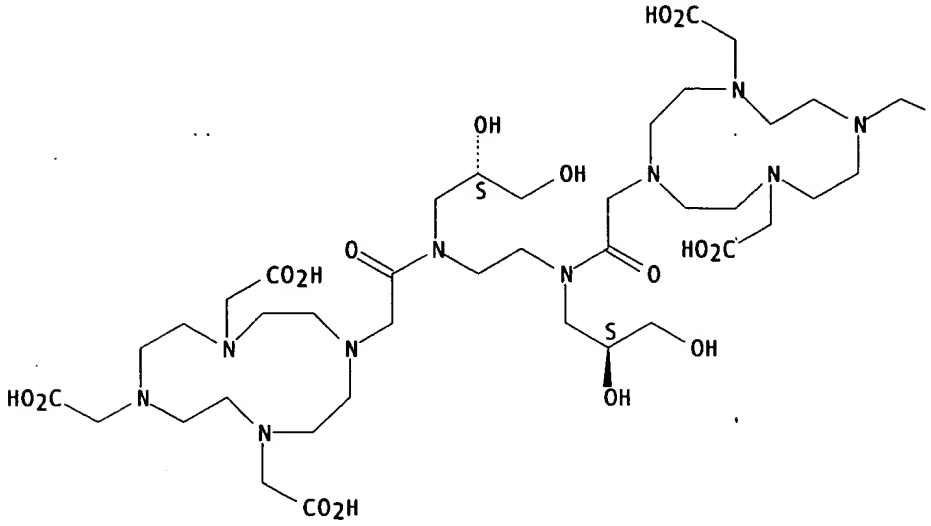
4667713 NRS=2
L7 101 L5 AND NRS=2

=> d scan

L7 101 ANSWERS REGISTRY COPYRIGHT 2001 ACS
IN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[[(2,3-dihydroxypropyl)imino](2-oxo-2,1-ethanediyl)]]bis-, [S-(R*,R*)]- (9CI)
MF C40 H72 N10 O18

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

CO2H

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	142.40	142.55

FILE 'CAPLUS' ENTERED AT 10:15:46 ON 26 FEB 2001

FILE COVERS 1967 - 26 Feb 2001 VOL 134 ISS 10
FILE LAST UPDATED: 25 Feb 2001 (20010225/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

  This file supports REGistRY for direct browsing and searching of
  all substance data from the REGISTRY file. Enter HELP FIRST for
  more information.

Now you can extend your author, patent assignee, patent information,
and title searches back to 1907. The records from 1907-1966 now have
this searchable data in CAOLD. You now have electronic access to all
of CA: 1907 to 1966 in CAOLD and 1967 to the present in CAPLUS on STN.

The CA Lexicon is now available in the Controlled Term (/CT) field.
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searching databases on STN. Any dissemination, distribution, copying,
or storing of this information, without the prior written consent of
CAS, is strictly prohibited.

=> d his

     (FILE 'HOME' ENTERED AT 10:12:30 ON 26 FEB 2001)

     FILE 'REGISTRY' ENTERED AT 10:12:37 ON 26 FEB 2001
L1   SCREEN 2076
L2   STRUCTURE UPLOADED
L3   QUE L2 AND L1
L4   11 S L3
L5   308 S L3 SSS FUL
L6   80 S L5 AND NRS=1
L7   101 S L5 AND NRS=2

     FILE 'CAPLUS' ENTERED AT 10:15:46 ON 26 FEB 2001

=> s l6

L8   52 L6

=> s l7

L9   52 L7

=> s l8 or l9

L10   83 L8 OR L9

=> d his

     (FILE 'HOME' ENTERED AT 10:12:30 ON 26 FEB 2001)

     FILE 'REGISTRY' ENTERED AT 10:12:37 ON 26 FEB 2001
L1   SCREEN 2076
L2   STRUCTURE UPLOADED
L3   QUE L2 AND L1
L4   11 S L3
L5   308 S L3 SSS FUL
L6   80 S L5 AND NRS=1
L7   101 S L5 AND NRS=2

     FILE 'CAPLUS' ENTERED AT 10:15:46 ON 26 FEB 2001
L8   52 S L6

```
L9            52 S L7
L10           83 S L8 OR L9

=> d l3

L3 HAS NO ANSWERS
L1              SCR 2076
L2              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L3              QUE  ABB=ON  PLU=ON  L2 AND L1


=> d ibib abs hitstr l10 1-83


L10  ANSWER 1 OF 83  CAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:661180  CAPLUS
DOCUMENT NUMBER:          133:249059
TITLE:                    Radionuclide conjugates with DOTA-biotin derivatives
                          for diagnosis and therapy
INVENTOR(S):              Griffiths, Gary L.; Hansen, Hans; Govindan, Serengulam
                          V.
PATENT ASSIGNEE(S):       Immunomedics, Inc., USA
SOURCE:                   U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 486,166,
                          abandoned.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   11
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     US 6120768         A    20000919       US 1997-990843   19971215
     US 5736119         A    19980407       US 1995-409960   19950323
     US 5922302         A    19990713       US 1995-440652   19950515
     WO 9930745         A2   19990624       WO 1998-US26579  19981215
     WO 9930745         A3   20000113
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
             US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9918258         A1   19990705       AU 1999-18258    19981215
PRIORITY APPLN. INFO.:                     US 1993-62662    19930517
                                           US 1995-409960   19950323
                                           US 1995-486166   19950607
                                           US 1996-688781   19960731
                                           US 1997-990843   19971215
                                           WO 1998-US26579  19981215
AB   A radionuclide-chelator conjugate compn. for detecting and/or treating
     lesions in a patient comprises pre-targeting the cell, tissue, or pathogen
     with a substrate, using a targeting protein that specifically binds a
     marker substance on the target cell, tissue, or pathogen and to which the
     substrate is directly or indirectly bound.  Parenteral injection comprises
     a chelate conjugate of biotin, a chelator, and a chelatable detection or
     therapeutic agent, and allows the compn. to accrete at the targeted cell,
     tissue, or pathogen.  The chelate conjugate is purified by liq. chromatog.
     after chelate formation, or further comprises a blood transit-modifying
     linker or addend that is covalently bound within the chelate conjugate, or
     both.  The detection or therapeutic agent of the invention are used to
     detect or treat cancer, infectious diseases, or cardiovascular diseases.
     Prepn. of biotin-D-Phe-D-Lys-DOTA is presented.
```
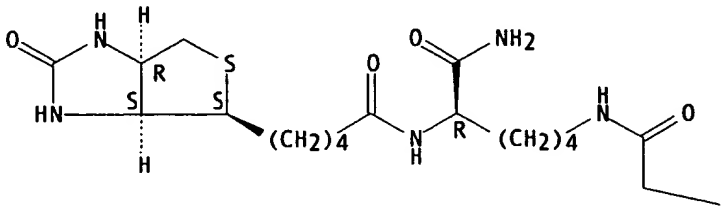

IT **192221-17-3P 192221-19-5P 245758-39-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(radionuclide conjugates contg. DOTA-biotin derivs. for diagnosis and therapy)

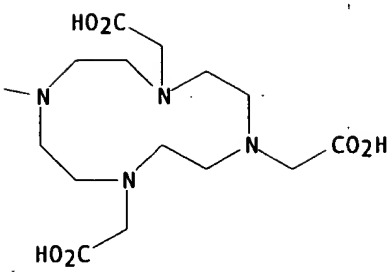
RN 192221-17-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(5R)-6-amino-5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



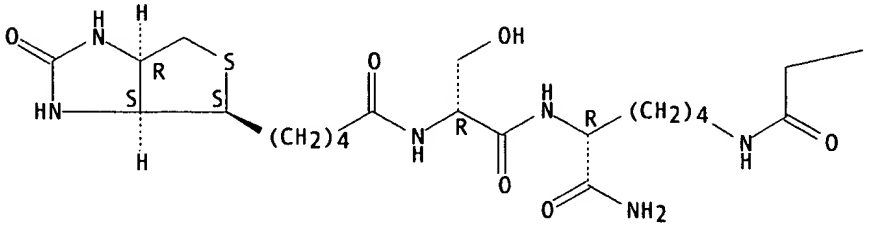
PAGE 1-B



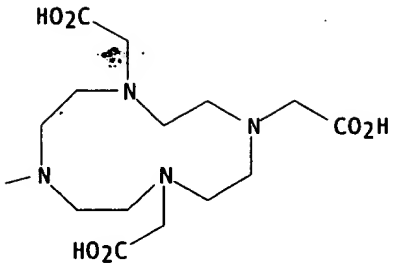
RN 192221-19-5 CAPLUS
CN D-Lysinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-D-seryl-N6-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



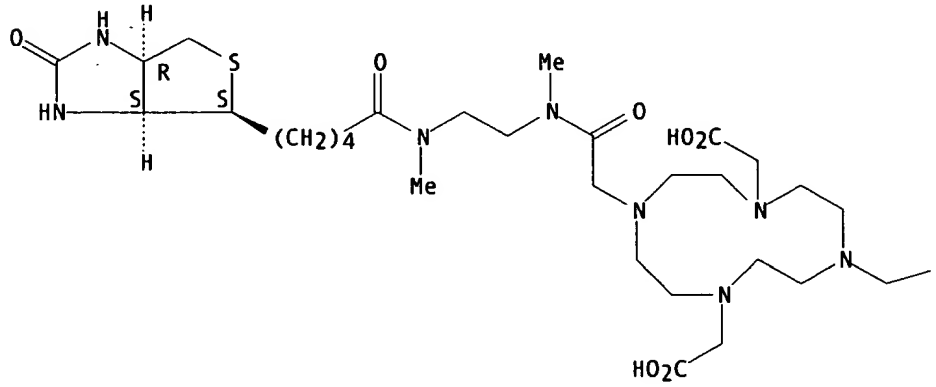
PAGE 1-B



RN 245758-39-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]methylamino]ethyl]methylamino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 31
REFERENCE(S): (1) Anon; WO 9114458 1991 CAPLUS
(2) Anon; EP 496074 1992 CAPLUS
(3) Anon; WO 9325240 1993 CAPLUS
(4) Anon; WO 9515335 1995 CAPLUS
(5) Bos; Cancer Research 1994, V54, P3479 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:514839 CAPLUS
DOCUMENT NUMBER: 133:260685
TITLE: Non-covalent conjugates between cationic polyamino

acids and GdIII chelates: a route for seeking accumulation of MRI-contrast agents at tumor targeting sites

AUTHOR(S): Aime, Silvio; Botta, Mauro; Garino, Elena; Crich, Simonetta Geninatti; Giovenzana, Giovanni; Pagliarin, Roberto; Palmisano, Giovanni; Sisti, Massimo

CORPORATE SOURCE: Dipartimento di Chimica I.F.M. Universita di Torino, Turin, 10125, Italy

SOURCE: Chem.--Eur. J. (2000), 6(14), 2609-2617
CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH

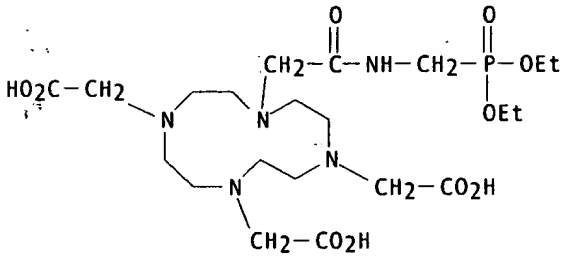
DOCUMENT TYPE: Journal

LANGUAGE: English

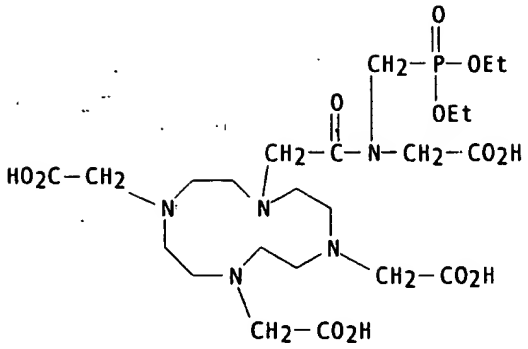
AB Three novel Gd chelates contg. on their external surface pendant phosphonate and carboxylate groups, which promote the interaction with the pos. charged groups of polyornithine and polyarginine, were synthesized. Their soln. structures were assessed from 1H- and 31P-NMR spectra of the Eu and Yb analogs. A thorough investigation of the relaxometric (1H and 17O) properties of the Gd chelates was carried out and the obsd. relaxivities were accounted for the sum of three contributions arising from water mols. in the 1st, 2nd, and outer coordination layers, resp. The occurrence of a tight 2nd coordination coating renders the dissocn. of the water mol. directly coordinated to the Gd ion more difficult. The binding interactions between the neg. charged Gd chelates and the pos. charged groups of polyornithine (.apprx.140 residues) and polyarginine (.apprx.204 residues) were evaluated by the proton relaxation enhancement (PRE) method. Although the binding interaction decreases markedly in the presence of competitive anions in the soln. medium, the affinity is strong enough that in blood serum it is possible to meet the conditions where most of the chelate is bound to the polyamino acid substrate. On this basis one may envisage a novel route for a MRI location of tumors as pos. charged polyamino acids selectively bind to tumors having a greater neg. charge than nontumor cells.

IT **294630-10-7P 294630-12-9P 294630-14-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and chelation with rare earths as potential MRI contrast agents)

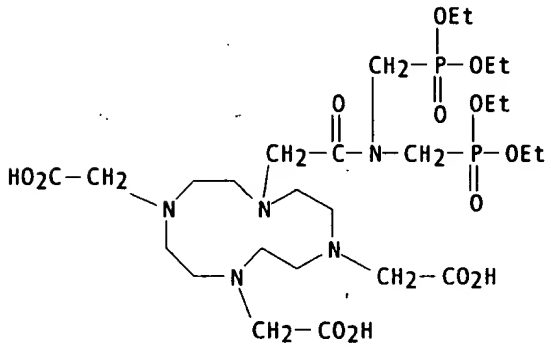
RN 294630-10-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(diethoxyphosphinyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 294630-12-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(carboxymethyl)[(diethoxyphosphinyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 294630-14-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[bis[(diethoxyphosphinyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25
REFERENCE(S): (1) Aime, S; Acc Chem Res 1999, V32, P941 CAPLUS
(2) Aime, S; Chem Soc Rev 1998, V27, P19 CAPLUS
(3) Aime, S; Inorg Chem 1992, V31, P2422 CAPLUS
(4) Aime, S; Inorg Chem 1992, V31, P4291 CAPLUS
(5) Aime, S; Inorg Chem 1997, V36, P2059 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:456934 CAPLUS
DOCUMENT NUMBER: 133:98665
TITLE: Preparation of metal complexes of polyaminopolycarboxylate linked bile acid derivatives as blood pool agents for nuclear magnetic resonance diagnostics
INVENTOR(S): Anelli, Pier Lucio; Brocchetta, Marino; De Haen, Christoph; Gazzotti, Ornella; Lattuada, Luciano; Lux, Giovanna; Manfredi, Giuseppe; Morosini, Pierfrancesco; Palano, Daniela; Serleti, Michele; Uggeri, Fulvio; Visigalli, Massimo
PATENT ASSIGNEE(S): Bracco International B.V., Neth.; et al.
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038738	A1	20000706	WO 1999-EP10002	19991216

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 1998-MI2802 19981223
OTHER SOURCE(S): MARPAT 133:98665
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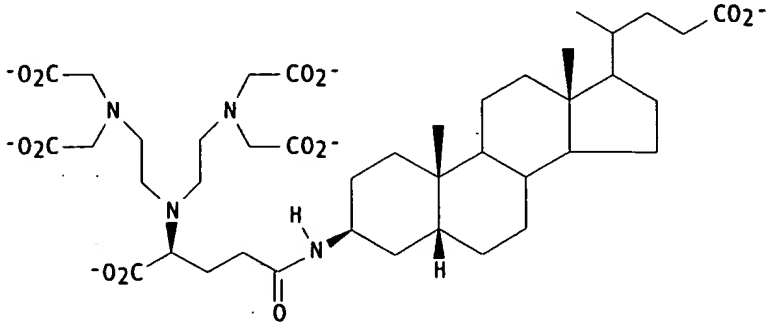


I

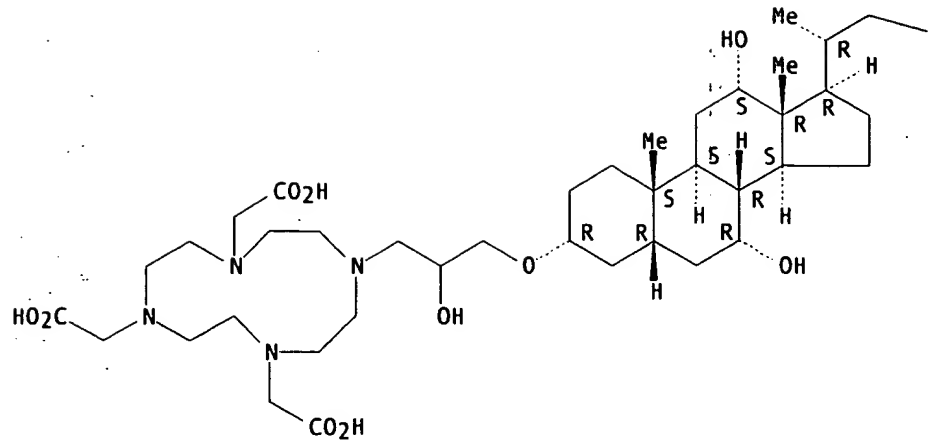
AB The prepn., use and diagnostic compns. are described for complexes of X-L-Y (I) with paramagnetic bi-trivalent metal ions selected from the group consisting of Fe(2+), Fe(3+), Cu(2+), Cr(3+), Gd(3+), Eu(3+), Dy(3+), Yb(3+) or Mn(2+), as well as the salts thereof with physiol. compatible org. bases selected from primary, secondary, tertiary amines or basic amino acids; or with inorg. bases whose cations are sodium, potassium, magnesium, calcium or mixts. thereof. In X-L-Y, X is the residue of a polyaminopolycarboxylic ligand and the derivs. thereof, selected from the group consisting of: EDTA, DTPA, DOTA, DO3A, BOPTA; Y is the deriv. of a bile acid selected from the group consisting of residues of cholic, chenodeoxycholic, deoxycholic, ursodeoxycholic, lithocholic acids, both as they are and functionalized at the positions having the hydroxy group as the reactive group; L is a chain linked at any position of X and the C-3, C-7, C-12 positions of Y. The complexes may be used for the imaging of the blood system of the human and animal body, by NMR. Thus, [GdL](Q)3 (L = II, Q = methylglucammonium) was prepd. and its applicability for use as an MRI imaging agent demonstrated by measuring the relaxation rate of rabbit blood.

IT **174267-83-5D**, transition metal complexes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of metal complexes of polyaminopolycarboxylate linked bile acid derivs. as blood pool agents for NMR diagnostics)

RN 174267-83-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-23-carboxy-7,12-dihydroxy-24-norcholan-3-yl]oxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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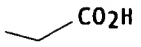


REFERENCE COUNT: 5
REFERENCE(S):
(1) Abbott Lab; EP 0279307 A 1988 CAPLUS
(2) Betebenner, D; Bioconjugate Chem 1991, V2(2), P117 CAPLUS
(3) Hoechst AG; EP 0417725 A 1991 CAPLUS
(4) Lucio, A; WO 9532741 A 1995 CAPLUS
(5) Peter, M; WO 9519186 A 1995 CAPLUS

L10 ANSWER 4 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:426648 CAPLUS
DOCUMENT NUMBER: 133:246448
TITLE: Conjugates of cyclodextrins with charged and neutral macrocyclic europium, terbium and gadolinium complexes: sensitised luminescence and relaxometric investigations and an example of supramolecular relaxivity enhancement
AUTHOR(S): Skinner, Philip J.; Beeby, Andrew; Dickins, Rachel S.; Parker, David; Aime, Silvio; Botta, Mauro
CORPORATE SOURCE: Department of Chemistry, University of Durham, Durham, DH1 3LE, UK
SOURCE: Perkin 2 (2000), (7), 1329-1338
CODEN: PRKTFO
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis and characterization of lanthanide complexes of mono- and tetra-amide .beta.-cyclodextrin derivs. of 1,4,7,10-tetraazacyclododecanetetraacetate (DOTA) are reported. Luminescence and relaxivity measurements confirm that the Eu, Tb and Gd complexes of the eight-coordinate mono-amide ligand possess one bound H2O mol. while the tetra-amide complexes are rare examples of q = 0 systems in aq. soln. The relaxivity of the host .beta.-CD Gd complex (8.50 mM-1 s-1, 20 MHz, 298 K) is enhanced when noncovalently bound to a 2nd Gd complex bearing two Ph moieties with an enhancement that is limited by the slowness of the H2O exchange rate (.tau.m = 0.6 .mu.s, 298 K). Sensitization of the Tb luminescence in the mono-amide .beta.-CD complex occurs in the absence of O using various substituted naphthalene derivs. (e.g. naphthalene, K = 1.04 .times. 104 M-1, 293 K) and Me p-tert-butylbenzoate. The slowness of the intra-complex energy transfer step severely limits the efficiency of this process and restricts the scope of 'noncovalently triggered luminescence' to a narrow range of guest substrates, as deduced by variable temp. time-resolved luminescence and flash-photolysis studies.

IT 293294-62-9P

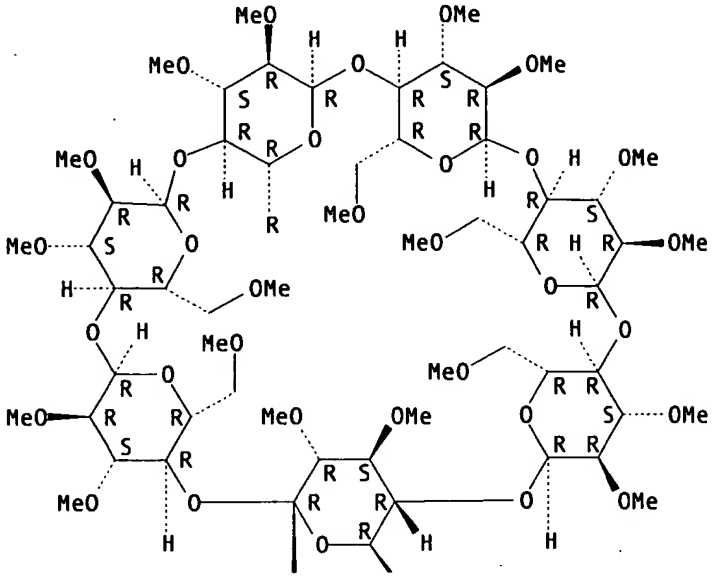
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with lanthanides)

RN 293294-62-9 CAPLUS

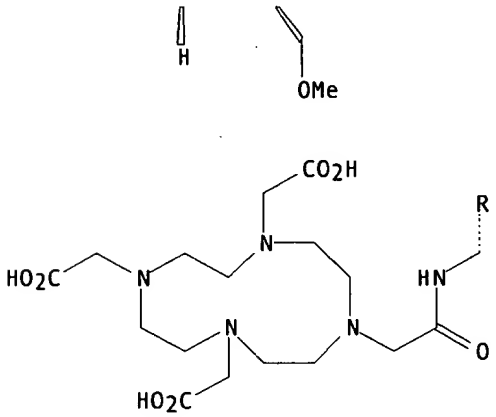
CN .beta.-Cyclodextrin, 6A-deoxy-2A,2B,2C,2D,2E,2F,2G,3A,3B,3C,3D,3E,3F,3G,6B,6C,6D,6E,6F,6G-eicosa-O-methyl-6A-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 62

REFERENCE(S):

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(2) Aime, S; Chem Soc Rev 1998, V27, P19 CAPLUS
(4) Aime, S; J Am Chem Soc 1999, V121, P5762 CAPLUS
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(6) Bates, P; J Chem Soc, Chem Commun 1993, P693 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:368157 CAPLUS

DOCUMENT NUMBER: 133:26120

TITLE: Preparation of amphipatic polycarboxylic paramagnetic

metal chelates as MRI contrast agents

INVENTOR(S): Anelli, Pier Lucio; Lattuada, Luciano; Uggeri, Fulvio; Lux, Giovanna; Serleti, Michele; Gabellini, Milena; Tournier, Herve

PATENT ASSIGNEE(S): Bracco International B.V., Neth.

SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000030688	A2	20000602	WO 1999-IB1889	19991125
WO 2000030688	A3	20001109		

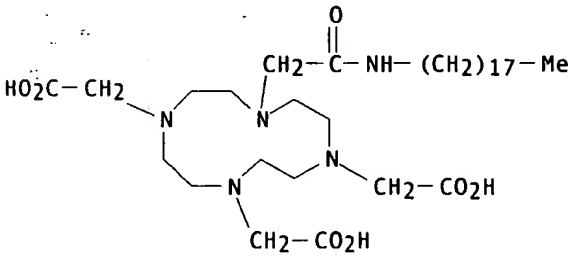
W: JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: EP 1998-203997 19981126
OTHER SOURCE(S): MARPAT 133:26120

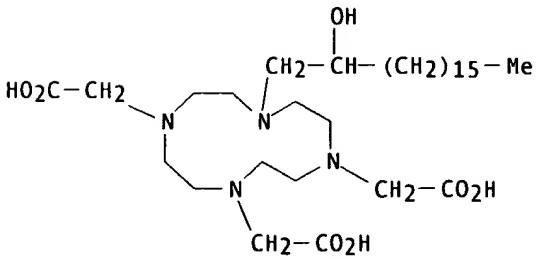
AB R2CHR(CO)n[CH(OH)]mR1 [R = C12-15 (un)satd. hydrocarbyl, alkyl, alkylene (sic); R1 = NHR3, NR4R5, OR6, R9. O2R9, etc.; R2 = 4,7,10-tris(carboxymethyl)-1,4,7,10 tetraazacyclododecan-1-yl; R3-R6 = (O-interrupted)(oxo)hydrocarbyl, etc.; R9 = (heteroatom-interrupted)(oxo)hydrocarbyl], R13COCHR13[CH2CH2N(CH2COR13)2]2 [R12 = (heteroatom-interrupted)(oxo)hydrocarbyl, etc.; R13 = OH, alkylamino, etc.], and Gd carboxylate salts thereof were prepd. as MRI contrast agents (no data). Thus, HOCH2CH2OCH2CH2NH2.HCl was esterified by stearoyl chloride and the product biamidated by N,N-bis[2-(2,6-dioxo-4-morpholinyl)ethyl]glycine to give, after (AcO)2Gd.bul.4H2O salification, Gd3+ -O2CH2N[CH2CH2N(CH2CO2-)CH2ONHCH2CH2OCH2CH2OR']2 (R' = stearoyl).

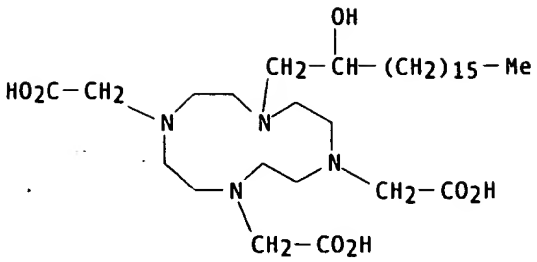
IT **259172-09-3P 272120-16-8P 272120-18-0P**
272120-43-1P 272120-45-3P 272120-47-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of amphipatic polycarboxylic paramagnetic metal chelates as MRI contrast agents)

RN 259172-09-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-(octadecylamino)-2-oxoethyl]- (9CI) (CA INDEX NAME)

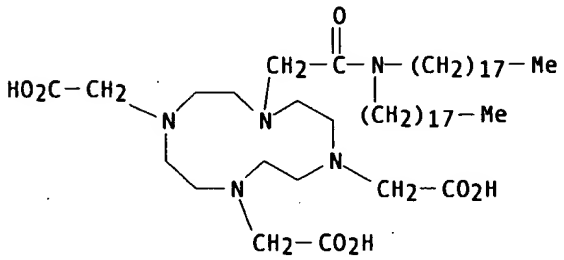


RN 272120-16-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxyoctadecyl)- (9CI) (CA INDEX NAME)



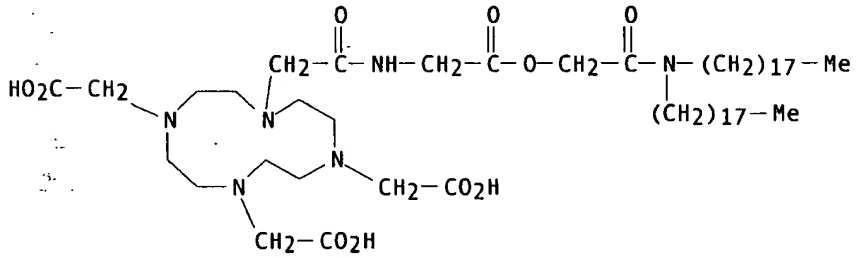


RN 272120-18-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-(dioctadecylamino)-2-oxoethyl]-, trihydrochloride (9CI) (CA INDEX NAME)

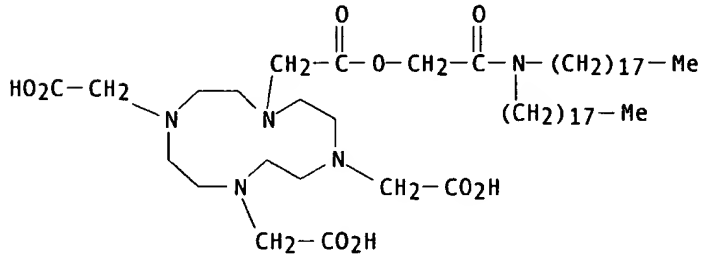


●3 HCl

RN 272120-43-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[2-(dioctadecylamino)-2-oxoethoxy]-2-oxoethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

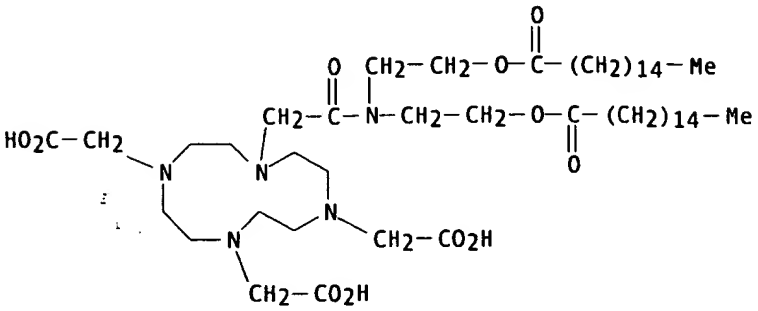


RN 272120-45-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, mono[2-(dioctadecylamino)-2-oxoethyl] ester (9CI) (CA INDEX NAME)



RN 272120-47-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[bis[2-[(1-

oxohexadecyl)oxy]ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 6 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:367158 CAPLUS
DOCUMENT NUMBER: 133:230264
TITLE: Experimental assessment of the efficacy of sensitized emission in water from a europium ion, following intramolecular excitation by a phenanthridinyl group
AUTHOR(S): Clarkson, Ian M.; Beeby, Andrew; Bruce, James I.; Govenlock, Linda J.; Lowe, Mark P.; Mathieu, Celine E.; Parker, David; Senanayake, Kanthi
CORPORATE SOURCE: Department of Chemistry, University of Durham, Durham, DH1 3LE, UK
SOURCE: New J. Chem. (2000), 24(6), 377-386
CODEN: NJCHE5; ISSN: 1144-0546
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The overall quantum yields for phenanthridinium sensitized emission from a Eu ion were measured in H2O and D2O for 5 structurally related, octadentate ligands in which the distance from the phenanthridinium chromophore to the Eu ion varies from 2.5 to .apprx.8.2 .ANG.. Overall quantum yields (pD.ltoreq.2) range from 0.25 to 0.012 suggesting that the exptl. distance for 50% efficiency of intramol. energy transfer lies close to 5.5 .ANG.for this system.
IT **291767-73-2P 291767-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(ligand; sensitized emission in water from europium ion following intramol. excitation by phenanthridinyl group)
RN 291767-73-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(6-butyl-2-phenanthridinyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

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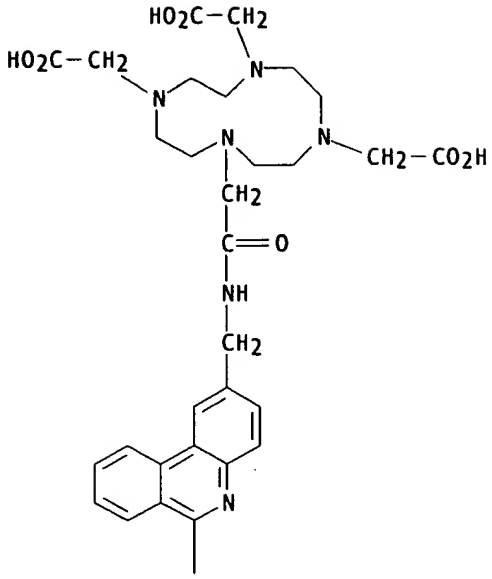

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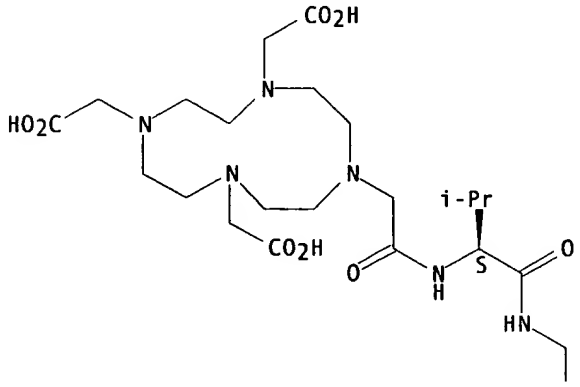
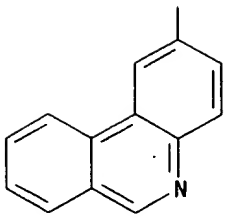
RN 291767-77-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(1S)-2-methyl-1-[[(2-phenanthridinylmethyl)amino]carbonyl]propyl]amino]-2-oxoethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 33
REFERENCE(S):
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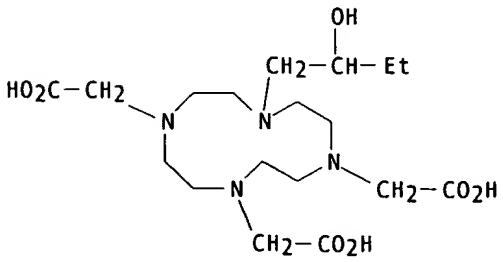
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:292443 CAPLUS
DOCUMENT NUMBER: 133:98615
TITLE: Synthesis and physicochemical characterisation of new amphiphilic gadolinium DO3A complexes as contrast agents for MRI
AUTHOR(S): Glogard, Christian; Hovland, Ragnar; Fossheim, Sigrid L.; Aasen, Arne J.; Klaveness, Jo
CORPORATE SOURCE: Blindern, School of Pharmacy, Department of Medicinal Chemistry, University of Oslo, Oslo, N-0317, Norway
SOURCE: Perkin 2 (2000), (5), 1047-1052
CODEN: PRKTFO
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two approaches were employed in the syntheses of four 1,4,7-tris(carboxymethyl)-10-(2-hydroxyalkyl)-1,4,7,10-tetraazacyclododecanes (4) with alkyl = Bu, octyl, dodecyl, hexadecyl. Physicochem. properties, such as crit. micelle concn. (CMC), micelle size, partition coeff. (P) between H2O and octan-1-ol and T1 relaxivity (r1), were studied for the corresponding Gd complexes. The Gd complexes contg. the shortest alkyl chains (Bu and octyl) showed properties typical of water-sol. Gd complexes. However, the long-chained chelates with dodecyl and hexadecyl possess amphiphilic properties and form micelles. The relaxivities of these amphiphilic complexes are concn. dependent, consistent with the formation of micelles. An unexpectedly high relaxivity was measured for the Gd complex with the hexadecyl chain below its CMC. This feature is probably caused by cluster formation due to low soly. in H2O.

IT 281188-68-9P 281188-69-0P 281188-70-3P
281188-71-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with gadolinium)
RN 281188-68-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxybutyl)- (9CI) (CA INDEX NAME)



RN 281188-69-0 CAPLUS
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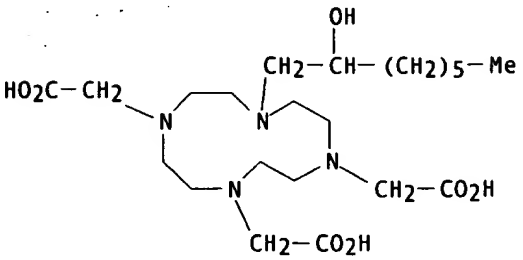
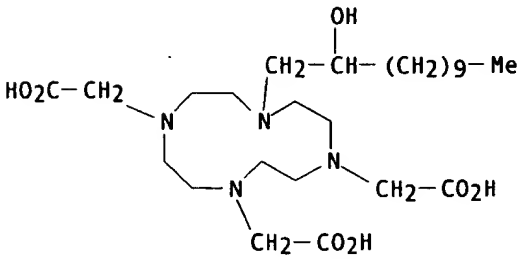
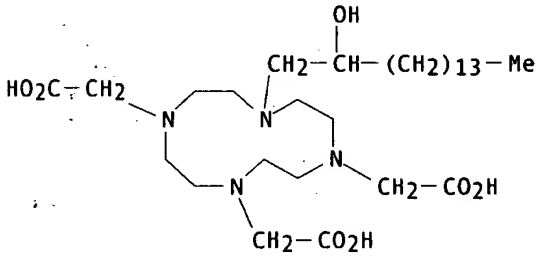


RN 281188-70-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxydodecyl)- (9CI) (CA INDEX NAME)



RN 281188-71-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxyhexadecyl)- (9CI) (CA INDEX NAME)



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REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:278271 CAPLUS
DOCUMENT NUMBER: 133:146994
TITLE: Macrocyclic Chelators with Paramagnetic Cations Are Internalized into Mammalian Cells via a HIV-Tat Derived Membrane Translocation Peptide
AUTHOR(S): Bhorade, Rajeev; Weissleder, Ralph; Nakakoshi, Tsunenori; Moore, Anna; Tung, Ching-Hsuan

CORPORATE SOURCE: Center for Molecular Imaging Research, Massachusetts General Hospital Harvard Medical School, Charlestown, MA, 02129, USA
SOURCE: Bioconjugate Chem. (2000), 11(3), 301-305
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A major obstacle to using paramagnetic MR contrast agents for in vivo cell tracking or mol. sensing is their generally low cellular uptake. In this study, we show that a paramagnetically labeled DOTA chelator derivatized with a 13-mer HIV-tat peptide is efficiently internalized into mammalian cells. Intracellular concns. were attained that were readily detectable by MR imaging using both gadolinium and dysprosium chelates. Using this paradigm, it should be feasible to internalize a variety of chem. different agents into mammalian cells.

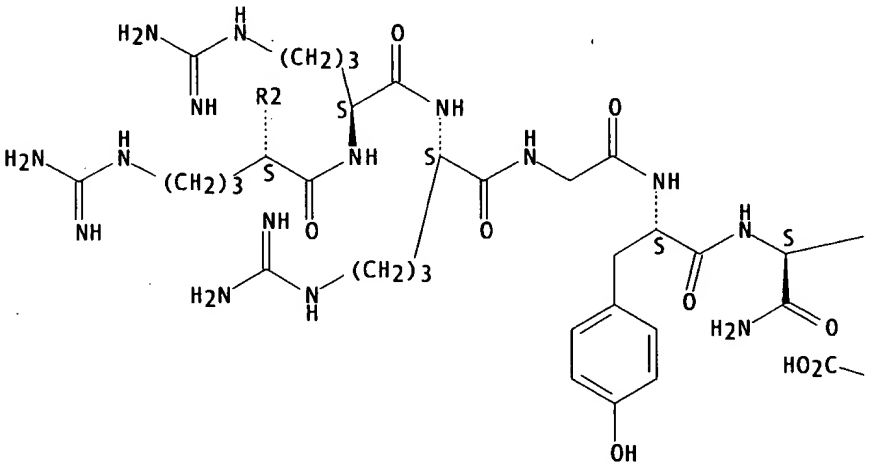
IT **287101-86-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(macrocyclic chelators with paramagnetic cations are internalized into mammalian cells via a HIV-Tat-derived membrane translocation peptide)

RN 287101-86-4 CAPLUS

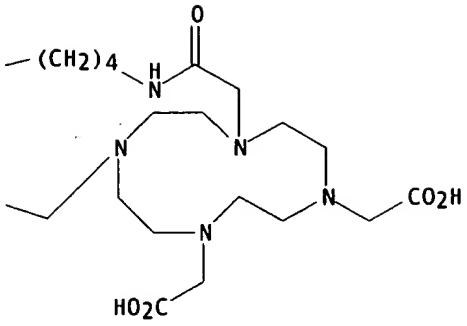
CN L-Lysinamide, glycyl-L-arginyl-L-lysyl-L-lysyl-L-arginyl-L-arginyl-L-glutaminyl-L-arginyl-L-arginyl-L-arginylglycyl-L-tyrosyl-N6-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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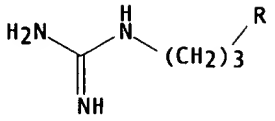

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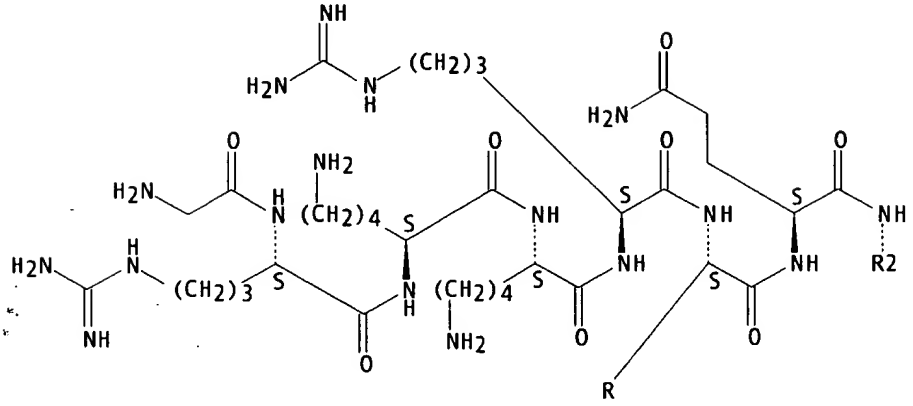

REFERENCE COUNT: 37
REFERENCE(S):
(1) Anderson, D; Biochem Biophys Res Commun 1993, V194, P876 CAPLUS
(2) Antopolsky, M; Bioconjugate Chem 1999, V10, P598 CAPLUS
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(4) Bayley, H; Nat Biotechnol 1999, V17, P1066 CAPLUS
(5) Cleves, A; Curr Biol 1997, V7, PR318 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:275379 CAPLUS
DOCUMENT NUMBER: 132:302529
TITLE: Preparation of ion pairs of dinuclear metal complexes of linked 4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecanes and their use as contrast

means.
INVENTOR(S): Bauer, Michael; Maier, Franz; Krause, Werner
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

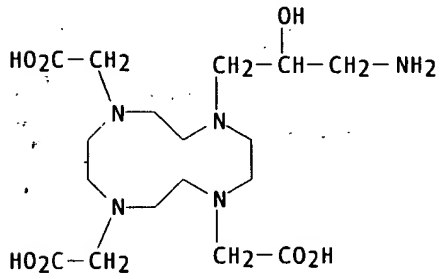
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19849465	A1	20000427	DE 1998-19849465	19981021

OTHER SOURCE(S): MARPAT 132:302529

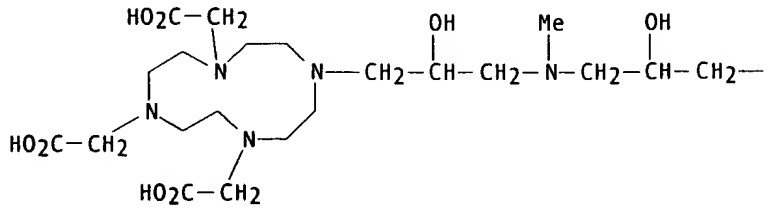
AB The prepn. of ion pairs of metal dinuclear complexes of 1,1'-(R-substituted)bis(4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane) (R = (non)branched C2-9-alkylene groups substituted with 1-2 O atoms and/or 1-3 N atoms and/or substituted with 1-5 OH groups and/or contg. 1-2 carboxy, phosphonate or sulfonyl moieties; metal = rare earth, transition metal, Group IVA, Group VA, Ca) is claimed. For example, (1,1'-dihydroxy-4-aza-2,6-heptanediyl)bis[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane]didysprosium 1,1'-[1,7-dihydroxy-4-aza-N-(4-carboxy-3-aza-1-oxobutyl)-2,6-heptanediyl]bis[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane]didysprosate was prepd. in a 7-step process. These complexes can be used in MRI diagnostics and radiotherapy.

IT **146270-94-2DP**, metal complexes as ion pairs with other similar coordination compds. **264598-78-9DP**, metal complexes as ion pairs with other similar coordination compds. **264598-79-0DP**, metal complexes as ion pairs with other similar coordination compds. **264598-82-5DP**, metal complexes as ion pairs with other similar coordination compds. **264598-83-6DP**, metal complexes as ion pairs with other similar coordination compds.
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use in radiotherapy and as MRI agents)

RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



RN 264598-78-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[(methylimino)bis(2-hydroxy-3,1-propanediyl)]bis- (9CI) (CA INDEX NAME)



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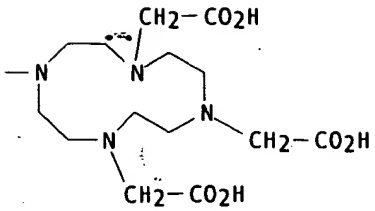

RN 264598-79-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[iminobis(2-hydroxy-3,1-propanediyl)]bis- (9CI) (CA INDEX NAME)

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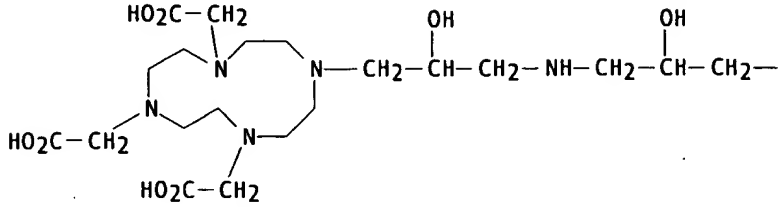
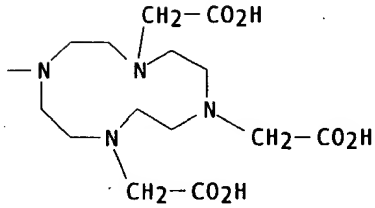
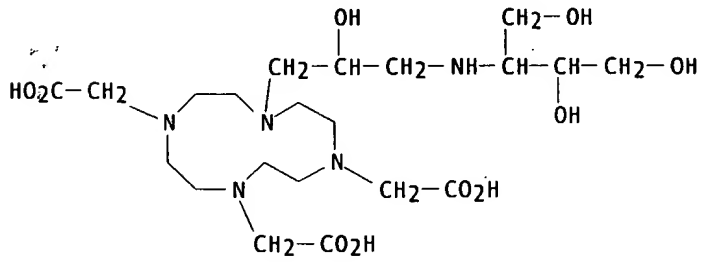


PAGE 1-B

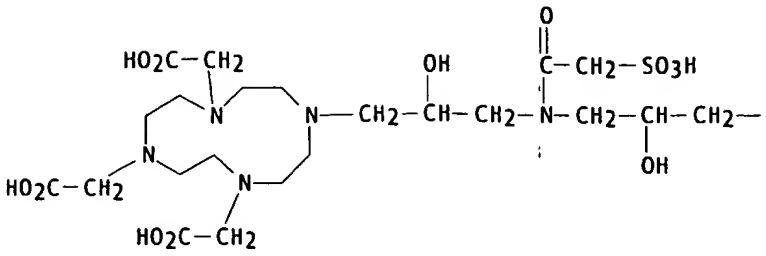


RN 264598-82-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[2,3-dihydroxy-1-(hydroxymethyl)propyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 264598-83-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[[(sulfoacetyl)imino]bis(2-hydroxy-3,1-propanediyl)]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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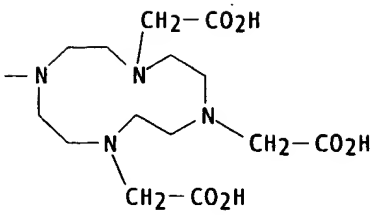


REFERENCE COUNT: 3
REFERENCE(S): (1) Anon; EP 0255471 A1 CAPLUS
(2) Anon; EP 0485045 A2 CAPLUS
(3) Anon; WO 9507270 A1 CAPLUS

L10 ANSWER 10 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:198520 CAPLUS
DOCUMENT NUMBER: 133:9331
TITLE: Force Field Parametrization for Gadolinium Complexes Based on ab Initio Potential Energy Surface Calculations
AUTHOR(S): Villa, Alessandra; Cosentino, Ugo; Pitea, Demetrio; Moro, Giorgio; Maiocchi, Alessandro
CORPORATE SOURCE: Dipartimento di Scienze dell'Ambiente e del Territorio, Universita degli Studi di Milano-Bicocca, Milan, 20126, Italy
SOURCE: J. Phys. Chem. A (2000), 104(15), 3421-3429
CODEN: JPCAFH; ISSN: 1089-5639
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

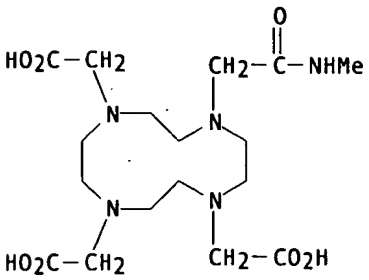
AB. The recent design of new magnetic resonance imaging (MRI) contrast agents is oriented toward the synthesis of gadolinium(III) complexes with ligands presenting formally neutral (amidic or alc.) or anionic (phosphinic) oxygen donor atoms. This paper presents the mol. mechanics (MM) parametrization of Gd interactions with amidic, alc. and phosphinic oxygen donor atoms, with the aim of supporting exptl. effort. The parametrization is performed on the basis of a previously developed procedure applied to the parametrization of Gd interactions with polyamino carboxylate (PAC) ligands. Within the framework of valence force fields, the parameters for Gd-ligand interactions are detd. by fitting the empirical potential to the ab initio potential energy surface (PES) of [Gd.cntdot.3.cntdot.OH2]3+, [Gd.cntdot.5b.cntdot.OH2]3+, and [Gd.cntdot.8a]1-. Ab initio calcns. were performed at the RHF (RHF) level by using an effective core potential (ECP) that includes 4f electrons in the core, an optimized valence basis set for the metal, and the 3-21G basis set for the ligand. Sampling of the PES is performed by moving the ion into the frozen coordination cage of the ab initio optimized geometries. The energy and first derivs., with respect to the Cartesian coordinates of the metal and donor atoms, were calcd. for each generated structure. Two sets of parameters, with the electrostatic contribution turned on or off in the force fields, were detd. To test the quality of

the derived parameters and their transferability to other Gd complexes, MM calcns. were performed on several gadolinium complexes. The results show that both sets of parameters provide reliable mol. geometries, but it is necessary to include the electrostatic contribution in the force fields to correctly reproduce the conformational energies.

IT 120041-07-8
RL: PRP (Properties)
(force field parametrization for gadolinium complexes based on ab initio potential energy surface calcns.)

RN 120041-07-8 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-(methylamino)-2-oxoethyl]- (9CI) (CA INDEX NAME)

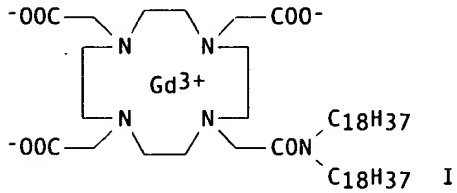


REFERENCE COUNT: 34
REFERENCE(S): (1) Aime, S; Inorg Chem 1992, V31, P2422 CAPLUS
(2) Aime, S; Inorg Chem 1994, V33, P4696 CAPLUS
(3) Aime, S; J Am Chem Soc 1999, V121, P5762 CAPLUS
(4) Alderighi, L; Eur J Inorg Chem 1998, P1581 CAPLUS
(5) Beech, J; Struct Chem 1996, V7, P153 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:133574 CAPLUS
DOCUMENT NUMBER: 132:185427
TITLE: Combination of a positive MRI contrast agent with a negative MRI contrast agent
INVENTOR(S): Tournier, Herve; Hyacinthe, Roland
PATENT ASSIGNEE(S): Bracco Research S.A., Switz.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009170	A1	20000224	WO 1999-IB1378	19990804
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:			EP 1998-810766	19980810

GI

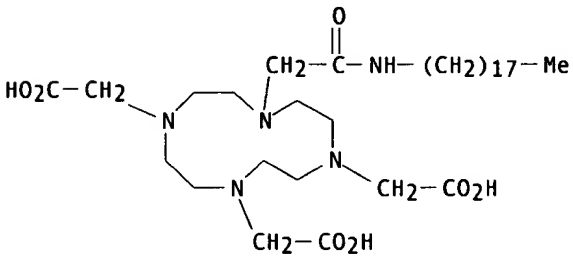


AB A first object of the invention is to provide administrable dual MRI

contrast enhancing compns. contg. as key components, at least (a) one pos. paramagnetic metal chelate contrast agent and at least (b) one neg. ferromagnetic or superparamagnetic contrast agent. These compns. distinguish the prior art by the properties of the said components toward the cell membrane barrier. Actually, either one of (a) and (b) predominantly internalizes tissue, whereas the remaining one is predominantly retained in the circulation, this being for a time sufficient to provide sharp MRI images of the circulation in said tissue. Typically, either one of (a) and (b) is predominantly intra-vascular while the other one is predominantly extra-vascular or is rapidly removed from the circulation by macrophages. Then, after removal from circulation it internalizes neighboring tissue. The transfer from vessels to tissues is effected by RES mediated phagocytosis. Alternatively, an extravascular compd. may cross the vessel walls and distribute randomly extracellularly. Another object of the invention is to provide is to provide a dual blood pool contrast medium comprising a pos. MRI contrast agent (a) mainly shortening the T1 relaxation response and a neg. contrast agent (b) mainly shortening the T2 relaxation response, both relaxation effects of (a) and (b) being controllable at will. One example compd. prepd. was I.

IT 259172-09-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(combination of a pos. MRI contrast agent with a neg. MRI contrast agent)

RN 259172-09-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-(octadecylamino)-2-oxoethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16
REFERENCE(S):
(2) Dekang, S; US 5312617 A 1994 CAPLUS
(3) Evan, U; US 5320826 A 1994 CAPLUS
(5) Henrik, T; WO 9702842 A 1997 CAPLUS
(6) Julian, C; WO 8909625 A 1989 CAPLUS
(7) Julian, C; WO 9502831 A 1995 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:78838 CAPLUS
DOCUMENT NUMBER: 132:145790
TITLE: Oligomeric gadolinium azamacrocycle compounds that contain perfluoroalkyl, process for their production, and their use as NMR contrast agents and as radiotherapeutic agents
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduchel, Bernd; Schlecker, Wolfgang; Weinmann, Hanns-joachim; Frenzel, Thomas; Misselwitz, Bernd; Ebert, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: U.S., 32 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6019959	A	20000201	US 1998-106146	19980629

PRIORITY APPLN. INFO.: US 1997-54417 19970731

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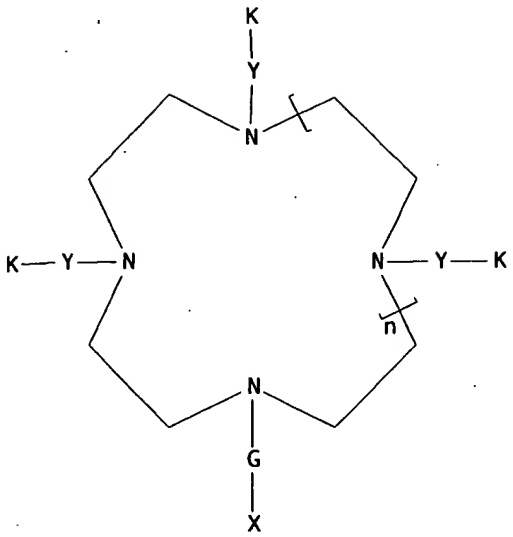


I

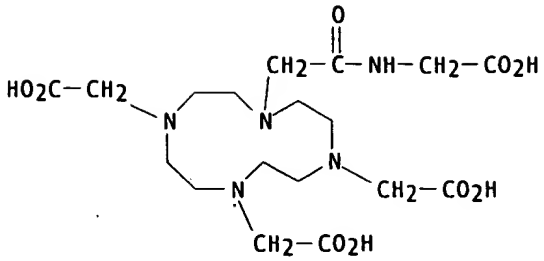
AB Claimed are oligomeric compds. A-RF that contain perfluoroalkyl in which A is a mol. portion that contains 2-6 metal complexes connected directly or via a linker to a N atom of an annular skeleton chain, RF is a perfluorinated, strait-chain or branched C chain with formula -CnF2nE (E = terminal F, Cl, Br, iodo, or H, n = 4-30), and A has azamacrocycle structure I [n = 0-3; K = complexing agent or metal complex, or their salts of org./inorg. bases, amino acids, or amino acid amides; X = direct bond to perfluoroalkyl group, phenylene, C1-C10 alkylene, etc.; Y = direct bond or chains defined by general structures -N(R1)-(CH2)k-(Z)l-(CH2)m-C(O)- or 1,3,5-trisubstituted (-NH-CH2C(O)NH)2C6H3-(CH2)0-5-C(O)-]. These compds. are useful as contrast agents in 1H NMR diagnosis and spectroscopy, x-ray diagnosis, radiodiagnosis, and as radiotherapeutic agents. The compds. are esp. suitable as blood pool contrast agents and as lymphatic system contrast agents. Gd compds. of the invention have surprisingly high proton relaxivity in comparison to com. available 1H NMR contrast media. An example prepd. trinuclear Gd complex, 1,4,7-tris{1,4,7-tris(N-carboxylatomethyl)-10-[N-(4,7-diaza-3,6,9-trioxo)nonane-2,9-diyl]-1,4,7,10-tetraazacyclododecane, Gd complex}-10-[N-acetyl-(2-amino-N-ethyl-N-perfluorooctylsulfonyl)]-1,4,7,10-tetraazacyclododecane, exhibits lymph node accumulations in guinea pigs which exceed those achieved with an extracellular contrast medium (Gd-DTPA) by a factor of 5-7. The blood elimination kinetics of example compds. were also evaluated.

IT **208253-06-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of oligomeric lanthanide azamacrocycle compds. contg. perfluoroalkyl group)

RN 208253-06-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(carboxymethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

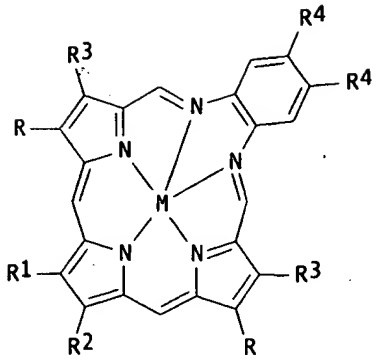


REFERENCE COUNT: 6
REFERENCE(S): (1) Kiefer; US 5834456 1998 CAPLUS
(3) Meyer; US 5712389 1998 CAPLUS
(4) Platzek; US 5690909 1997 CAPLUS
(5) Schmitt-Willich; US 5820849 1998 CAPLUS
(6) Tweedle; US 4885363 1989 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:15661 CAPLUS
DOCUMENT NUMBER: 132:87339
TITLE: New porphyrin derivative complexes having pharmaceutical metals for use in the photodynamic therapy and MRI diagnostics.
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduechel, Bernd; Weinmann, Hanns-Joachim; Frenzel, Thomas; Ebert, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19831217	A1	20000105	DE 1998-19831217	19980703
WO 2000001698	A1	20000113	WO 1999-EP4150	19990617
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9946111	A1	20000124	AU 1999-46111	19990617
US 6114321	A	20000905	US 1999-346891	19990702
PRIORITY APPLN. INFO.:			DE 1998-19831217	19980703
			US 1998-110696	19981203
			WO 1999-EP4150	19990617

OTHER SOURCE(S): MARPAT 132:87339
GI



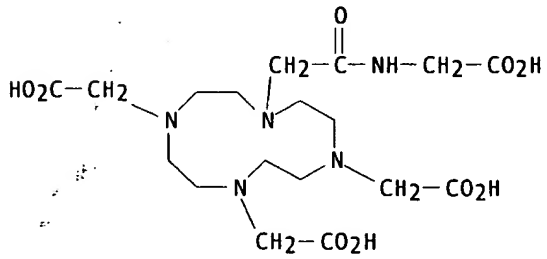
I

AB I [M = diamagnetic metal; R, R1, R2, R3 are independent of each other and are H, C1-30 alkyl contg. 1-10 O atoms or substituted with 1-5 hydroxy groups or 1-2 CO2H groups; R4 is a moiety contg. a linker of C1-20 alkyl having amino, carbonyl or carbamido or carbonylamino or S or phenylene groups and a chelating moiety of diethylenetriaminepentaacetic acid derivs. or 1,4,7,10-tetraazacyclododecanetetraacetic acid derivs.] were claimed for use in photodynamic therapy and MRI diagnostics. Thus the Lu,Gd dinuclear complex of N,N'-[9,10-diethyl-5,14-bis(3-hydroxypropyl)-4,15-dimethyl-8,11-imino-3,6:16:13-dinitrilo-1,18-benzodiazacycloeicosin-20,21-diyl]bis[({[oxy(1-oxopropan-1,3-diyl)imino]ethan-1,2-diyl}oxy)ethane-1,2-diyl]diamide of diethylenetriaminepentaacetic acid, in which Lu is coordinated in the pentaaza macrocycle and Gd is coordinated in the DPTA moiety, was prepd. in a multistep process. Other Lu-Gd and Gd-Zn complexes were prepd.

IT **208253-06-9**
RL: RCT (Reactant)
(reactant for prepn. of gadolinium/lutetium/zinc iminodinitrilobenzodiazacycloeicosine DTPA/tetraazacyclododecanetetraacetate deriv. heterotrinuclear complexes as MRI agents or photodynamic therapy)

RN 208253-06-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(carboxymethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 14 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:655849 CAPLUS

DOCUMENT NUMBER: 131:276952

TITLE: Delivery of diagnostic and therapeutic agents to a target site

INVENTOR(S): Griffiths, Gary L.; Hansen, Hans J.; Govindan, Serengulam V.; Karacay, Habibe

PATENT ASSIGNEE(S): Immunomedics, Inc., USA

SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Ser. No. 486,166, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5965131	A	19991012	US 1996-731107	19961009
CA 2223261	AA	19961219	CA 1996-2223261	19960607
US 5958408	A	19990928	US 1997-972037	19971117
PRIORITY APPLN. INFO.:			US 1995-486166	19950607
			US 1996-731107	19961009

AB An improvement in in vivo pretargeting methods for delivering diagnostic or therapeutic agents to a target site in a mammal uses a clearing agent that binds to the target-binding site of the targeting species, whereby the non-bound primary targeting species is cleared from circulation but the clearing agent does not remove the bound primary targeting species. Anti-idiotype antibodies and antibody fragments are preferred clearing agents. Fast clearance is achieved by glycosylating the clearing agent with sugar residues that bind to the hepatic asialoglycoprotein receptor.

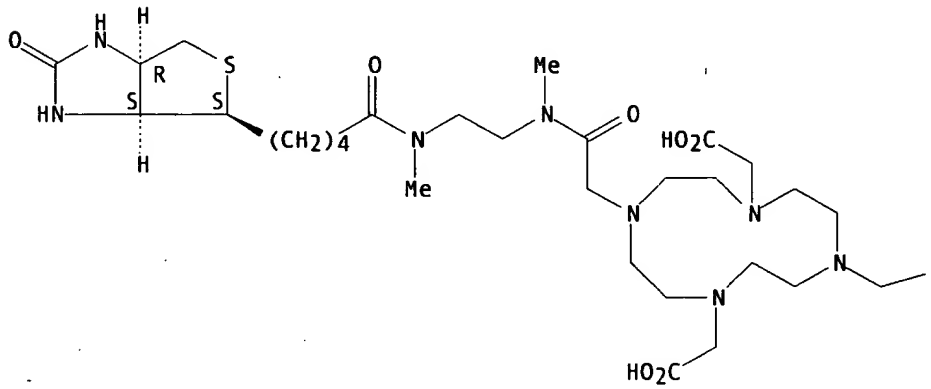
IT 245758-39-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery of diagnostic and therapeutic agents to a target site)

RN 245758-39-8 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]methylamino]ethyl]methylamino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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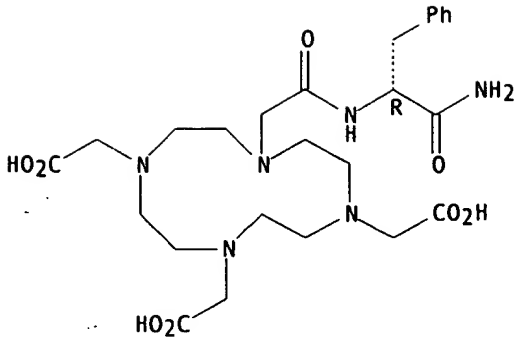
REFERENCE(S):

(1) Anon; WO 10140 1989
(2) Anon; Illustrated Dictionary of Immunology 1995, P24
(4) Goldenberg; US 5525338 1996 CAPLUS
(5) Goodwin; Cancer Research 1994, V54, P5937 CAPLUS
(7) Urdal, D; The Journal of Biological Chemistry

L10 ANSWER 15 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:442438 CAPLUS
DOCUMENT NUMBER: 131:239827
TITLE: Radiometal-labelled macrocyclic chelator-derivatized somatostatin analogue with superb tumour-targeting properties and potential for receptor-mediated internal radiotherapy
AUTHOR(S): Heppeler, A.; Froidevaux, S.; Macke, H. R.; Jermann, E.; Behe, M.; Powell, P.; Hennig, M.
CORPORATE SOURCE: Institute of Nuclear Medicine, Div. of Radiological Chemistry, University Hospital Basel, Basel, CH-4031, Switz.
SOURCE: Chem.--Eur. J. (1999), 5(7), 1974-1981
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A monoreactive DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) prochelator (4,7,10-tricarboxymethyl-tert-Bu ester 1,4,7,10-tetraazacyclododecane-1-acetate) was synthesized which is useful in solid-phase and soln.-phase peptide synthesis; it was coupled to the somatostatin analog Tyr3-Lys5(BOC)-octreotide. Deprotection in one step afforded DOTA0-D-Phe1-Tyr3-octreotide (DOTATOC) in .apprxeq.65% yield. This peptide, modified with a chelator, was complexed with the radiometals 67Ga3+, 111In3+ and 90Y3+ in high yields and with high specific activities. The three radiopeptides show high stability in human serum and high affinity to the somatostatin receptor: it is four to five times higher for 67Ga-DOTATOC compared to 90Y-DOTATOC and 111In-DOTATOC. The 67Ga-labeled compd. also shows significantly higher tumor and lower kidney uptake than the two congeners. 67Ga-DOTATOC was compared in patients with the com. available gold std. 111In-DTPA0-D-Phe1-octreotide. The new compd. delineates SRIF-receptor pos. tumors very favorably and shows distinctly lower uptake by the kidneys. Evidently, the differences in the coordination chem. of the metals causes the differences in the biol. behavior. Indeed, a crystallog. study of the Ga3+ and Y3+ complexes of the model peptide DOTA-D-PheNH2 showed differences in the geometry of the complexes. The gallium complex is hexacoordinated with pseudooctahedral cis geometry and a folded macrocyclic unit. The equatorial plane is formed by two transannular nitrogens of the cyclen ring and two oxygens of the corresponding carboxylate groups. The two axial positions are formed by the two remaining ring nitrogen atoms. The amide carboxy oxygen is not bound to the metal and one carboxylate group is free and most likely contributes to the favorable handling of the radiopeptide by the kidneys. In contrast, the structure of Y-DOTA-D-PheNH2 has eight-fold coordination, and includes the amide carboxy oxygen. The geometry is a compact and somewhat distorted square-antiprism with two almost perfect planes (N4 and O4) with a max. deviation of 0.025 A. The dihedral angle between the two planes is only 0.36.degree..
IT 244219-84-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and crystallog. study of Ga3+ and Y3+ complexes of DOTA-D-PheNH2)
RN 244219-84-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(1R)-2-amino-2-oxo-1-(phenylmethyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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REFERENCE(S):
(2) Aime, S; Angew Chem Int Ed 1998, V37, P2673 CAPLUS
(3) Aime, S; Chem Soc Rev 1998, V27, P19 CAPLUS
(4) Aime, S; Inorg Chem 1992, V31, P4291 CAPLUS
(5) Albert, R; Actualite de Chimie Therapeutique 1994, V21, P111 CAPLUS
(6) Albert, R; Bioorg Med Chem Letters 1998, V8, P1207 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:409606 CAPLUS
DOCUMENT NUMBER: 131:56136
TITLE: Dendritic polymer-saccharide conjugates and their preparation for use in NMR contrast media
INVENTOR(S): Berndorff, Dietmar; Mareski, Peter; Misselwitz, Bernd; Platzek, Johannes; Raduechel, Bernd; Weinmann, Hanns-Joachim
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 54 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19758105	A1	19990624	DE 1997-19758105	19971218
WO 9932154	A1	19990701	WO 1998-EP7927	19981209
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9922680	A1	19990712	AU 1999-22680	19981209
EP 1037672	A1	20000927	EP 1998-966256	19981209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

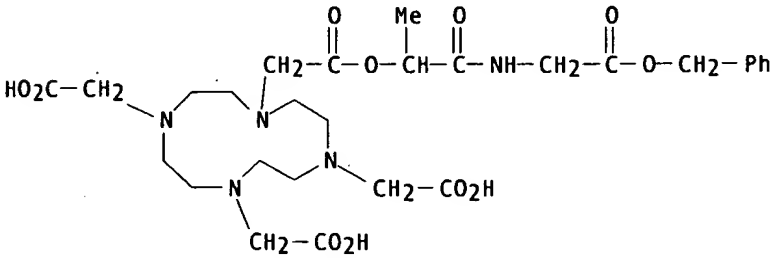
PRIORITY APPLN. INFO.: DE 1997-19758105 19971218
WO 1998-EP7927 19981209

AB The title conjugates, PKm(LZ)n (P = dendritic polymer with 12-150 amino groups; K = metal chelate group as detectable label; L = linker; Z = mono- or oligosaccharide group; m, n = 1-149), are excellent contrast agents for NMR diagnostics, esp. for lymphog. These conjugates are accumulated by the lymphatic system adequately for imaging, in some cases even sufficiently for morphol. differentiation of lymph nodes. They are relatively nontoxic, are excreted slowly (>98% in 14 days), and show a high relaxivity which allows their use in low dosages. Thus, a dendritic polyamine with 64 amino groups, of which 38 bore Gd-DTPA chelate groups and 26 were substituted with 1-(4-thioureidophenyl)-.alpha.-D-mannopyranosyl groups, when injected i.v. at 200 .mu.mol Gd/kg into rats, was accumulated in the liver, spleen, and esp. in the mesenteric and

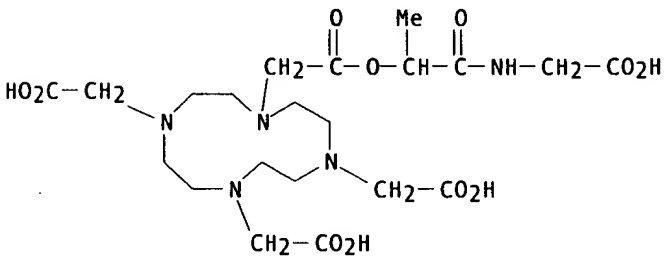
peripheral lymph nodes. Owing to the high relaxivity of this compd. in water (17.0 L/mmol s), a dose of .gtoreq.10 .mu.mol Gd/kg for i.v. NMR lymphog. is recommended. Prepn. of this and other contrast agents from the unsubstituted dendritic polyamines is described.

IT **228086-52-0P 228086-58-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(dendritic polymer-saccharide conjugates and their prepn. for use in NMR contrast media)

RN 228086-52-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, mono[1-methyl-2-oxo-2-[[2-oxo-2-(phenylmethoxy)ethyl]amino]ethyl] ester (9CI) (CA INDEX NAME)



RN 228086-58-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, mono[2-[(carboxymethyl)amino]-1-methyl-2-oxoethyl] ester (9CI) (CA INDEX NAME)



only 5 c's

L10 ANSWER 17 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:401701 CAPLUS
DOCUMENT NUMBER: 131:55892
TITLE: DOTA-biotin derivative metal complexes for therapeutic and diagnostic use using a pre-targeting protocol
INVENTOR(S): Griffiths, Gary L.; Hansen, Hans; Govindan, Serengulam V.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930745	A2	19990624	WO 1998-US26579	19981215
WO 9930745	A3	20000113		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6120768	A	20000919	US 1997-990843	19971215
AU 9918258	A1	19990705	AU 1999-18258	19981215
PRIORITY APPLN. INFO.:			US 1997-990843	19971215
			US 1993-62662	19930517
			US 1995-409960	19950323
			US 1995-486166	19950607
			US 1996-688781	19960731
			WO 1998-US26579	19981215

OTHER SOURCE(S): MARPAT 131:55892

AB A radionuclide-chelator conjugate compn. for detecting and/or treating lesions in a patient in a pre-targeting protocol comprises pre-targeting the target cell, tissue, or pathogen with a substrate, using a targeting protein that specifically binds a marker substance on the target cell, tissue, or pathogen and to which the substrate is directly or indirectly bound; parenterally injecting the detection or therapeutic compn. of the invention which comprises a chelate conjugate of biotin, a chelator, and a chelatable detection or therapeutic agent, and allowing the compn. to accrete at the targeted cell, tissue, or pathogen; wherein the chelate conjugate is purified by chromatog. after chelate formation, or further comprises a blood transit-modifying linker or addend that is covalently bound within the chelate conjugate, or both; and using the detection or therapeutic agent to detect or treat the targeted cell, tissue, or pathogen.

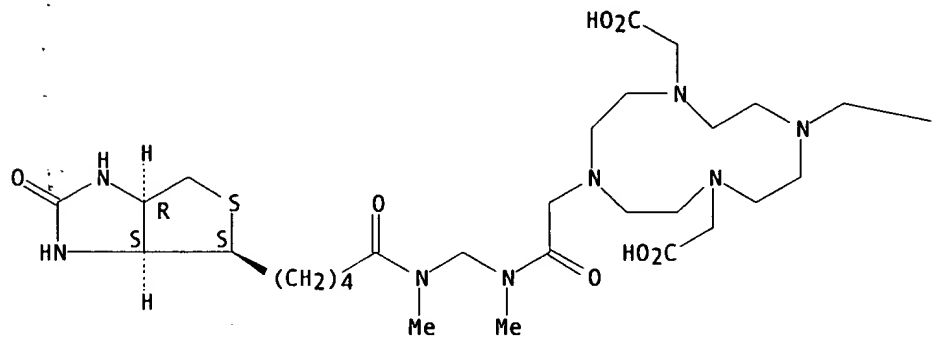
IT **227948-65-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DOTA-biotin deriv. metal complexes for therapeutic and diagnostic use using a pre-targeting protocol)

RN 227948-65-4 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]methylamino]methyl]methylamino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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L10 ANSWER 18 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:401700 CAPLUS

DOCUMENT NUMBER: 131:56134

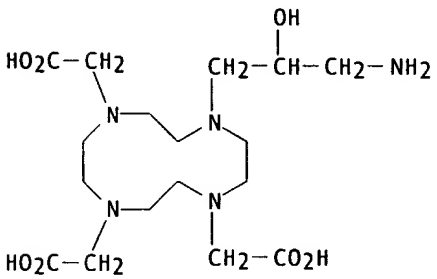
TITLE: Polyrotaxanes as contrast agents
INVENTOR(S): Platzek, Johannes; Schmitt-Willich, Heribert
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930744	A1	19990624	WO 1998-EP7924	19981209
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19758118	A1	19990701	DE 1997-19758118	19971217
AU 9921587	A1	19990705	AU 1999-21587	19981209
EP 1037671	A1	20000927	EP 1998-965773	19981209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6113880	A	20000905	US 1998-213287	19981217
PRIORITY APPLN. INFO.:			DE 1997-19758118	19971217
			US 1998-70703	19980107
			WO 1998-EP7924	19981209

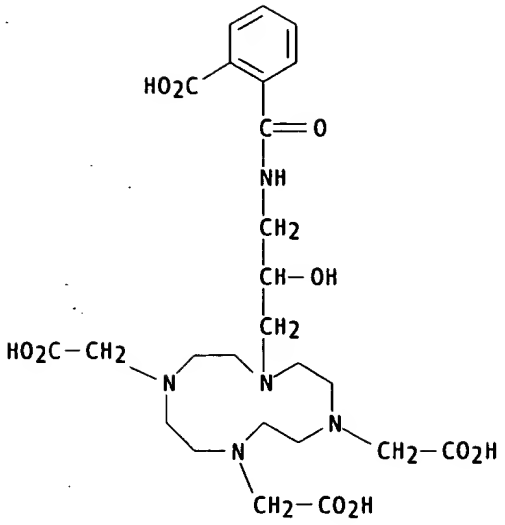
AB Polyrotaxanes which comprise 2-50 cyclic oligosaccharides threaded onto a linear polyoxyalkylene terminated with substituents .gtoreq.0.6 nm in diam., with metal complexes or triiodobenzoyl moieties as substituents on the cyclic oligosaccharides, are useful as contrast agents for MR tomog. and x-ray diagnosis. These compds., with a mol. wt. of 104-2 .times. 105, accumulate in regions of elevated vascular permeability (e.g. tumors), give information on perfusion of tissues and on blood vol., and are useful in angiog., lymphog., and diagnosis of inflammation. These polyrotaxanes, when used in MR imaging and diagnosis, can be 10-20% satd. with paramagnetic cations, compared to 5% for dextran chelate derivs. used previously. They can be administered parenterally in doses <1 mg/kg as solns. isoosmolar to blood, are relatively nontoxic, and are completely eliminated from the body. They are prepd. by reaction of cyclic oligosaccharides with H-terminated polyoxyalkylenes in a polar solvent, followed by functionalized terminating groups.

IT **146270-94-2P 174700-60-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(polyrotaxanes as contrast agents)

RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



RN 174700-60-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(2-carboxybenzoyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9
REFERENCE(S):
(2) Cardenas, D; Journal of the American Chemical Society 1997, V119(11), P2656 CAPLUS
(3) Harada, A; J Am Chem Soc 1994, V116, P3192 CAPLUS
(4) Harada, A; Macromolecules 1995, V28(24), P8406 CAPLUS
(5) Nihon Mediphysics Co Ltd; EP 0766968 A 1997 CAPLUS
(7) Platzek, J; WO 9801163 A 1998 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:313313 CAPLUS
DOCUMENT NUMBER: 131:127216
TITLE: Enzymatic Cleavage of Peptide-Linked Radiolabels from Immunoconjugates
AUTHOR(S): Peterson, James J.; Meares, Claude F.
CORPORATE SOURCE: Department of Chemistry, University of California, Davis, CA, 95616-5295, USA
SOURCE: Bioconjugate Chem. (1999), 10(4), 553-557
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

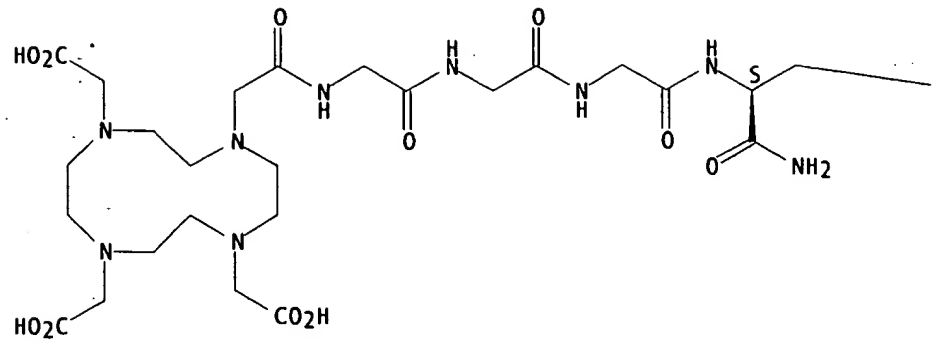
AB We have incorporated peptides selected by combinatorial library [Peterson, J. J., and Meares, C. F. (1998) Bioconjugate Chem. 9, 618-626] into peptide-linked radiolabeled immunoconjugates of the form DOTA-peptide-antibody. Decapeptide linkers -GFQGVQFAGF- and -GFGSVQFAGF-, selected for cleavage by human liver cathepsin B, were rapidly digested in vitro when compared to the simple model tetrapeptide motif of the prototype -GGGF- [Li, M., and Meares, C. F. (1993) Bioconjugate Chem. 4, 275-283]. Cleavage properties of these library-selected substrates for cathepsin B compared favorably with decapeptide linkers -GLVGGAGAGF- and -GGFLGLGAGF-, which incorporate two of the most labile extended cathepsin B substrates from the literature. The decapeptide linker -GFGSTFFAGF-, selected from the library for cleavage by human liver cathepsin D, was rapidly digested by cathepsin D while the others were not.

IT 149206-88-2DP, 90Y-labeled immunoconjugates 234442-94-5DP, 90Y-labeled immunoconjugates
RL: BPR (Biological process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(prepn. of 90Y-labeled DOTA-peptide-antibody conjugates and cleavage by cathepsin)

RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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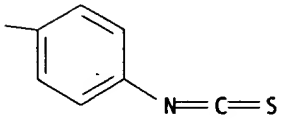
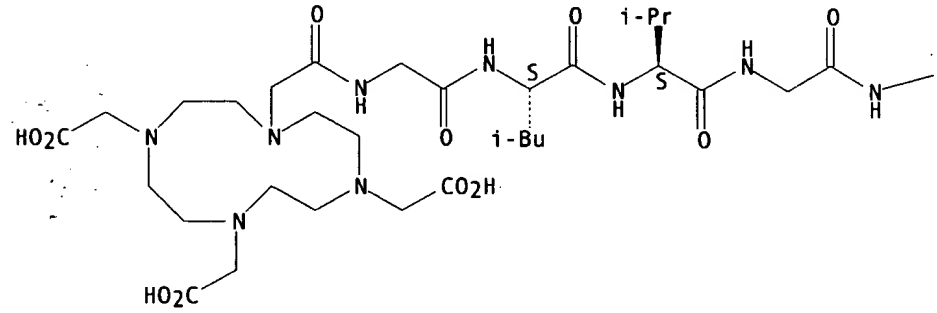


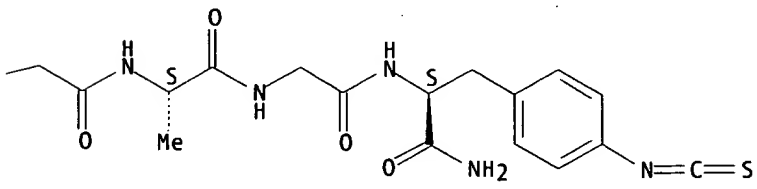
RN 234442-94-5 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycyl-L-leucyl-L-valylglycylglycyl-L-alanylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 44
REFERENCE(S):
(1) Arano, Y; Biconjugate Chem 1996, V7, P628 CAPLUS
(2) Arano, Y; Bioconjugate Chem 1998, V9, P497 CAPLUS
(3) Arano, Y; Nucl Med Biol 1994, V21, P63 CAPLUS
(4) Arano, Y; Nucl Med Biol 1995, V22, P555 CAPLUS
(5) Barrett, A; Biochem J 1967, V104, P601 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:233828 CAPLUS
DOCUMENT NUMBER: 130:278934
TITLE: Lipophilic metal complexes for necrosis and infarct imaging
INVENTOR(S): Platzek, Johannes; Speck, Ulrich; Niedballa, Ulrich; Raduechel, Bernd; Weinmann, Hanns-Joachim; Ebert, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

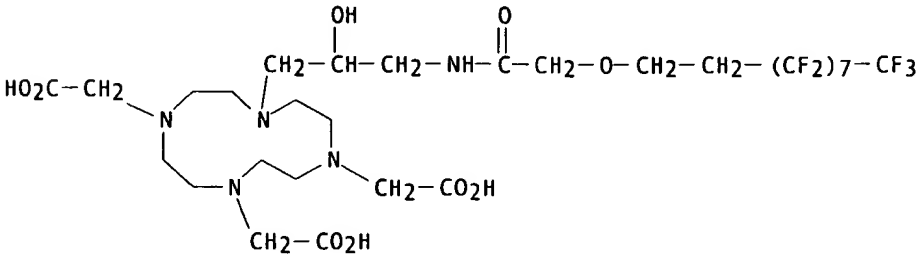
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9916474	A1	19990408	WO 1998-EP5185	19980817
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19744004	C1	19990722	DE 1997-19744004	19970926
AU 9892628	A1	19990423	AU 1998-92628	19980817
EP 1017424	A1	20000712	EP 1998-945248	19980817
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2000001520	A	20000525	NO 2000-1520	20000323
PRIORITY APPLN. INFO.:			DE 1997-19744004	19970926
			WO 1998-EP5185	19980817

AB Metal complexes with .gtoreq.10% (preferably .gtoreq.80%) plasma protein binding are useful as diagnostic imaging agents for locating an infarct or necrosis by formation of a persistent pos. (bright) image. The complexes have mol. wt. >350 Da, relaxivity >2.0 s-1 mM-1 at 20 MHz and 37.degree. in plasma, good water soly., and may contain a paramagnetic metal for NMR diagnosis or a radioactive metal for radiog. diagnosis. They show good stability in vitro and in vivo, and do not release significant amts. of toxic metal ions in vivo prior to excretion. The complexing agent is e.g. a polyaminopolycarboxylic acid, polyaminopolyphosphonic acid, porphyrin, texaphyrin, sapphyrin, or peptide. Thus, in rats with kidney infarcts induced by left renal artery occlusion, the infarcts were visualized by i.v. injection of the Gd complex, Eovist, and MRI tomog. 24 h later. The obsd. size of the necrotic region correlated well with that seen by histol. vital staining.

IT 222550-89-2D, metal complexes
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipophilic metal complexes for necrosis and infarct imaging)

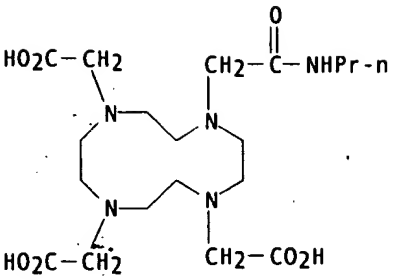
RN 222550-89-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)oxy]acetyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 14
REFERENCE(S): (1) Anon; US 5583220 A CAPLUS
(2) Anon; WO 9726017 A CAPLUS
(3) Board of Regents, The University of Texas System; WO 9510307 A 1995 CAPLUS
(4) Bracco Industria Chimica; EP 0230893 A 1987 CAPLUS
(5) Bracco Industria Chimica; EP 0325762 A 1989 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:186068 CAPLUS
DOCUMENT NUMBER: 131:16013
TITLE: NMR Studies of the Metal-Loading Kinetics and Acid-Base Chemistry of DOTA and Butylamide-DOTA
AUTHOR(S): Keire, David A.; Kobayashi, Mitsuo
CORPORATE SOURCE: The Beckman Research Institute of the City of Hope, Duarte, CA, 91010-0269, USA
SOURCE: Bioconjugate Chem. (1999), 10(3), 454-463
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The conjugation of a chelating agent to a protein via a covalent linkage has been previously reported to change the metal-binding characteristics of the chelator. A fundamental understanding of these binding changes would enable design of a new generation of metal-chelating agents for biol. applications. To assess the effect of conjugation on the commonly used chelating agent 1 4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA), we synthesized a model protein conjugate, 1,4,7-tris(carboxymethyl)-10-(butylaminocarboxymethyl)-1,4,7,10-tetraaazacyclododecane (BD) and explored the metal-binding characteristics via NMR. The extent of ionization of the carboxylic acid groups and the two protonated macrocycle nitrogens of DOTA and BD were detd. as a function of pH by chem. shift changes in proximal carbon-bonded protons. In addn. to the expected sensitivity of the chem. shifts to titrn. of proximate acidic groups, BD resonances from carbon-bonded protons 10-17 bonds distant from the deprotonation site also shifted significantly, indicating the presence of conformational changes. Furthermore, increased shielding of the amide and alkyl proton signals upon deprotonation of the carboxylic acid groups indicates the presence of pH-dependent hydrogen-bonded BD isoforms. On the basis of these NMR data, we propose new structures for the doubly protonated forms of DOTA and BD. To measure metal loading, the yttrium-loading rates (type I to type II) of DOTA and BD were detd. by following the intensity of type I and type II proton signals as a function of time. The yttrium-loading rates of BD are approx. one-half those of DOTA at pHs between 4.6 and 6.5 and 37 .degree.C. The loading rates measured as a function of pH indicate that while both the doubly protonated and singly protonated forms of DOTA are reactive to metal loading, only the singly protonated form of BD is reactive.
IT 118476-80-5P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. of butylamide-DOTA; NMR studies of metal loading kinetics, pKas, and structure of DOTA and the protein conjugate model compd. butylamide-DOTA)
RN 118476-80-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-(propylamino)ethyl]- (9CI) (CA INDEX NAME)



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(5) Bundi, A; Biopolymers 1979, V18, P299 CAPLUS
(6) Cacheris, W; Inorg Chem 1987, V26, P958 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:90012 CAPLUS
DOCUMENT NUMBER: 130:237860
TITLE: Total Solid-Phase Synthesis of 1,4,7,10-Tetraazacyclododecane-N,N',N'',N'''-tetraacetic Acid-Functionalized Peptides for Radioimmunotherapy
AUTHOR(S): Peterson, James J.; Pak, Roger H.; Meares, Claude F.
CORPORATE SOURCE: Department of Chemistry, University of California, Davis, CA, 95616-5295, USA
SOURCE: Bioconjugate Chem. (1999), 10(2), 316-320
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

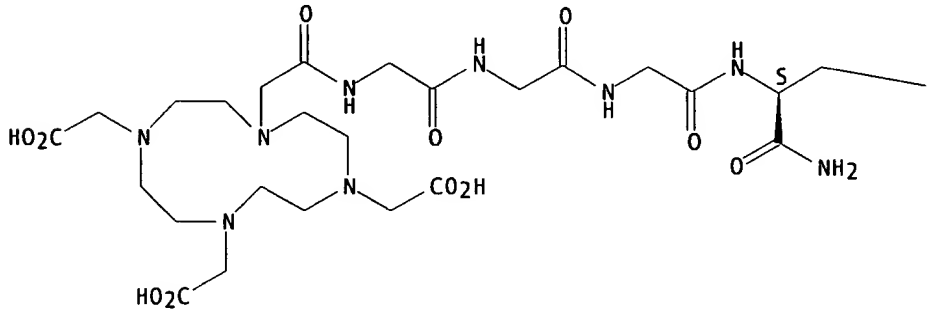
AB A convenient approach to the functionalization of peptides with the macrocyclic 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) moiety has been developed. Protected components (using tert-Bu or tert-butyloxycarbonyl groups) of both the peptide and the chelate were assembled on the same solid resin support. Deprotection and cleavage of the resin-bound DOTA-peptides were performed in one step using a trifluoroacetic acid cleavage mixt. to yield free DOTA-peptide amides.

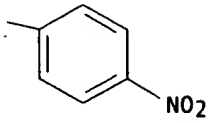
IT **149206-86-0P 221327-99-7P 221328-02-5P**
221328-07-0P 221328-08-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(total solid-phase synthesis of tetraazacyclododecanetetraacetic acid-functionalized peptides for radioimmunotherapy)

RN 149206-86-0 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

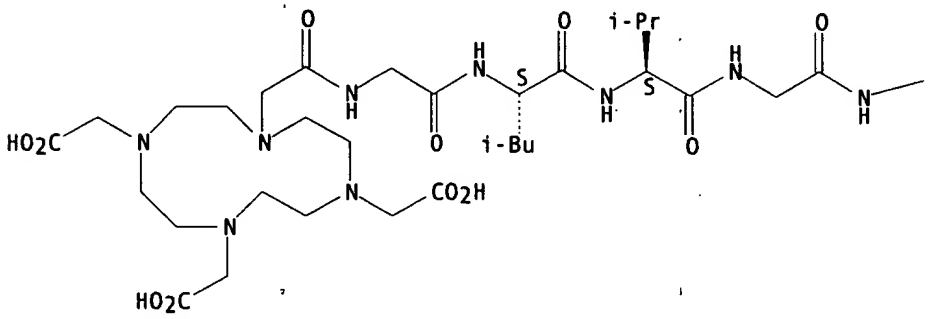




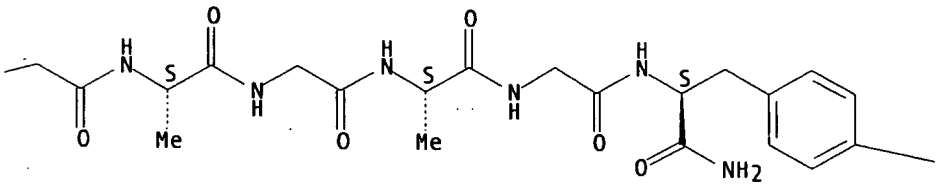
RN 221327-99-7 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycyl-L-leucyl-L-valylglycylglycyl-L-alanylglycyl-L-alanylglycyl-4-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

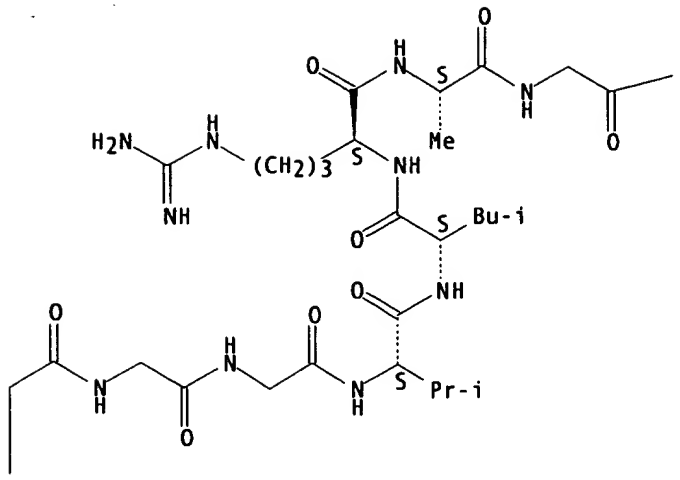


PAGE 1-C

RN 221328-02-5 CAPLUS
CN L-Lysinamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycyl-L-valyl-L-leucyl-L-arginyl-L-alanylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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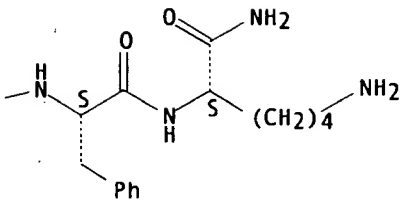
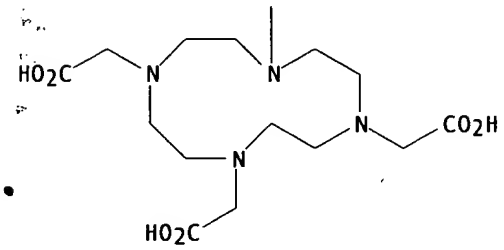


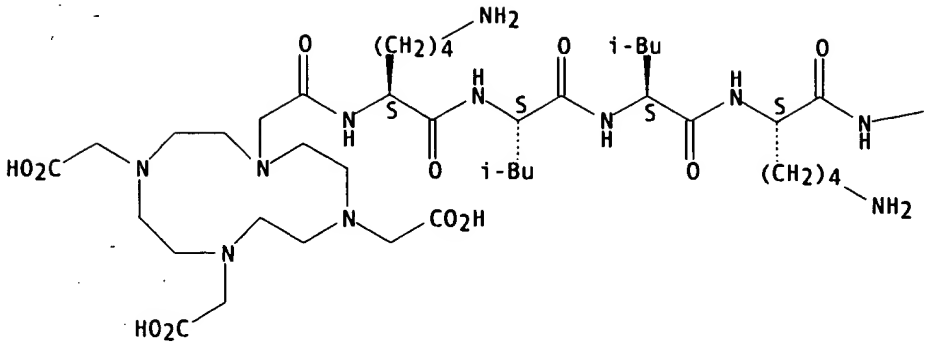
PAGE 2-A



RN 221328-07-0 CAPLUS
CN L-Lysinamide, N2-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]-L-lysyl-L-leucyl-L-leucyl-L-lysyl-L-leucyl-L-leucyl-L-leucyl-L-lysyl-L-leucyl-L-tyrosyl-L-lysyl-L-lysyl-L-leucyl-L-leucyl-L-lysyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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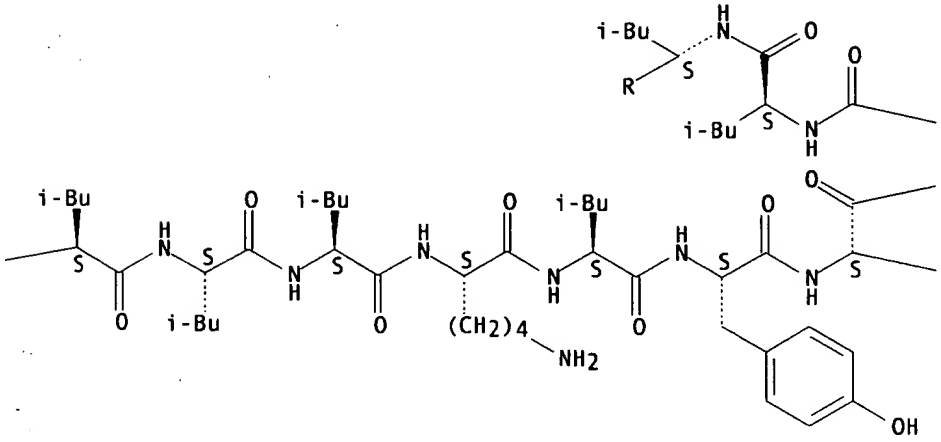
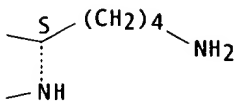
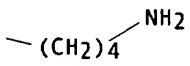
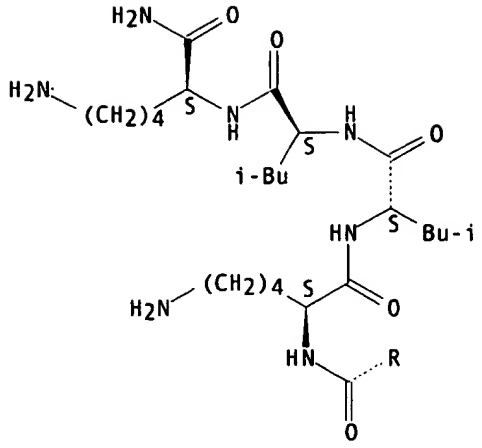


PAGE 1-C





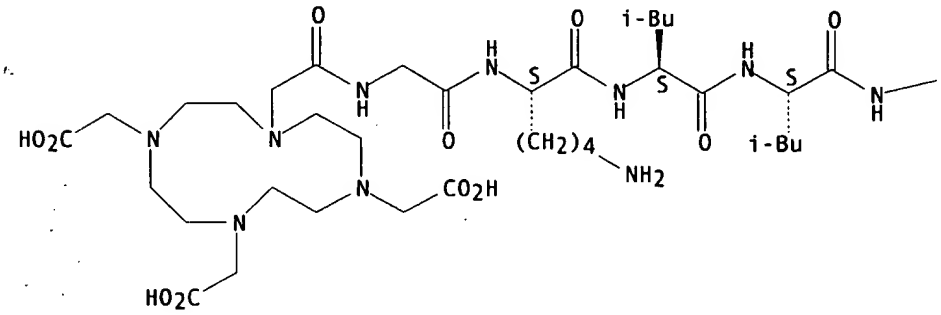
PAGE 2-A



RN 221328-08-1 CAPLUS
CN L-Lysinamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycyl-L-lysyl-L-leucyl-L-leucyl-L-lysyl-L-leucyl-L-leucyl-L-leucyl-L-lysyl-L-leucyl-L-tyrosyl-L-lysyl-L-lysyl-L-leucyl-L-leucyl-L-lysyl-L-leucyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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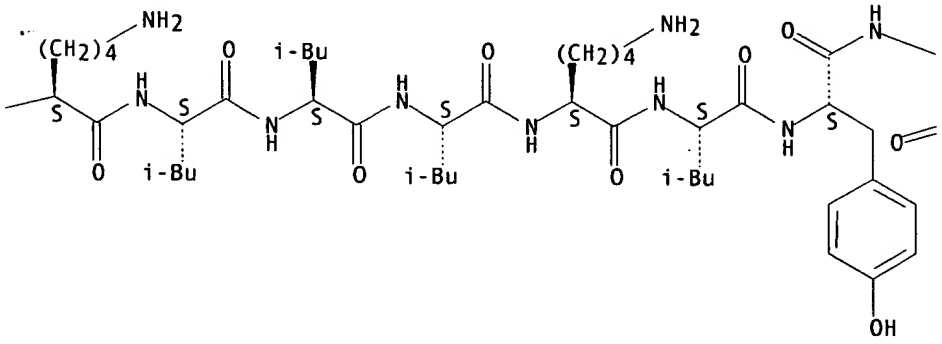
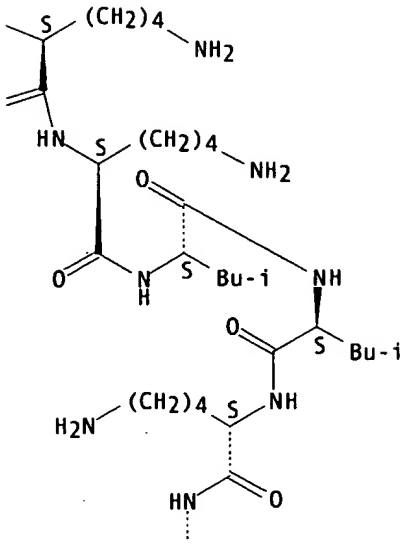
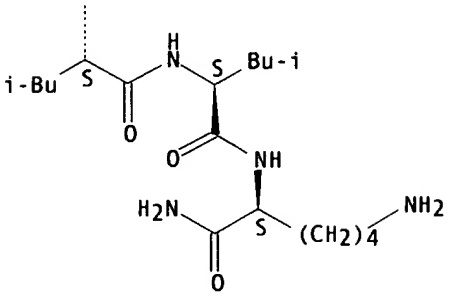






REFERENCE COUNT: 16
REFERENCE(S): (1) Cox, J; J Chem Soc Perkin Trans 1 1990, P2567 CAPLUS
(2) Desreux, J; Inorg Chem 1980, V19, P1319 CAPLUS
(3) Hudson, D; J Org Chem 1988, V53, P617 CAPLUS
(4) Kruper, W; J Org Chem 1993, V58, P3869 CAPLUS
(5) Lewis, M; Bioconjugate Chem 1994, V5, P565 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 23 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:53429 CAPLUS
DOCUMENT NUMBER: 130:136290
TITLE: Perfluoroalkylated oligomer compounds and their preparation for use in NMR diagnosis
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduechel, Bernd; Schlecker, Wolfgang; Weinmann, Hanns-Joachim; Frenzel, Thomas; Misselwitz, Bernd; Ebert, Wolfgang
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901161	A1	19990114	WO 1998-EP3143	19980528

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

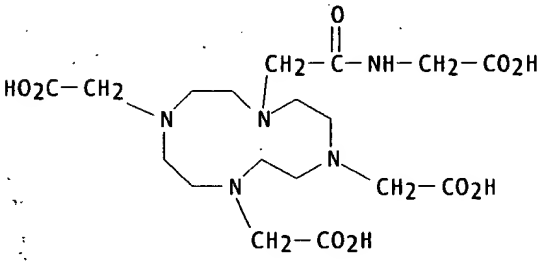
DE 19729013	A1	19990204	DE 1997-19729013	19970703
AU 9886236	A1	19990125	AU 1998-86236	19980528
EP 993306	A1	20000419	EP 1998-937424	19980528
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
ZA 9805895	A	19990416	ZA 1998-5895	19980703
PRIORITY APPLN. INFO.:			DE 1997-19729013	19970703
			WO 1998-EP3143	19980528

AB Perfluoroalkylated oligomer compds. ARF (A = moiety with 2-6 metal complexes bonded to an annular structural chain directly or via a linker with a N atom; RF = perfluorinated, straight or branched C chain CnF2nE; E = terminal F, Cl, Br, I, H; n = 4-30) are valuable for diagnosis, in particular as in-vivo NMR and x-ray contrast agents, as well as for radiodiagnosis and radiotherapy. Thus, 1,4,7,10-tetraazacyclododecane reacted with N-(benzyloxycarbonyl)glycine N-hydroxysuccinimide ester to form 1,4,7-tris[N-(benzyloxycarbonylamino)acetyl]-1,4,7,10-tetraazacyclododecane, which was then condensed with 2H,2H,4H,4H,5H,5H-3-oxaperfluorotridecanoic acid (prepn. given), deprotected, and condensed on N10 with 1,4,7-tris(N-carboxylatomethyl)-10-[N-(1-methyl-2-oxo-3-aza-4-carboxybutyl)]-1,4,7,10-tetraazacyclododecane Gd complex (prepn. given). The resulting Gd complex was administered i.v. to rats at 50 or 100 .mu.mol/kg for angiog. by NMR tomog.

IT 208253-06-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(perfluoroalkylated oligomer compds. and their prepn. for use in NMR diagnosis)

RN 208253-06-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(carboxymethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5
REFERENCE(S):
(1) Schering Ag; DE 4317588 A 1994 CAPLUS
(2) Schering Ag; DE 19521945 A 1996 CAPLUS
(3) Schering Ag; DE 19525924 A 1997 CAPLUS
(4) Schering Ag; DE 19603033 A 1997 CAPLUS
(5) Schering Ag; DE 19608278 A 1997 CAPLUS

L10 ANSWER 24 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:20744 CAPLUS
DOCUMENT NUMBER: 130:248789
TITLE: Optimized conditions for chelation of yttrium-90-DOTA immunoconjugates
AUTHOR(S): Kukis, David L.; DeNardo, Sally J.; DeNardo, Gerald L.; O'Donnell, Robert T.; Meares, Claude F.
CORPORATE SOURCE: Section of Radiodiagnosis and Therapy, Department of Internal Medicine, University of California Davis Medical Center, Sacramento, CA, USA
SOURCE: J. Nucl. Med. (1998), 39(12), 2105-2110
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Radioimmunotherapy (RIT) with 90Y-labeled immunoconjugates has shown promise in clin. trials. The macrocyclic chelating agent 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) binds 90Y with extraordinary stability, minimizing the toxicity of 90Y-DOTA immunoconjugates arising from loss of 90Y to bone. However, reported 90Y-DOTA immunoconjugate product yields have been typically only .ltoreq.50%. Improved yields are needed for RIT with 90Y-DOTA immunoconjugates to be practical. (S) 2-[p-(bromoacetamido)benzyl]-DOTA (BAD) was conjugated to the monoclonal antibody Lym-1 via 2-iminothiolane (2IT). The immunoconjugate product, 2IT-BAD-Lym-1, was labeled in excess yttrium in various buffers over a range of concns. and pH. Kinetic studies were performed in selected buffers to est. radiolabeling reaction times under prospective radiopharmacy labeling conditions. The effect of temp. on reaction kinetics was examd. Optimal radiolabeling conditions were identified and used in eight radiolabeling expts. with 2IT-BAD-Lym-1 and a second immunoconjugate, DOTA-peptide-chimeric L6, with 248-492 MBq (6.7-13.3 mCi) of 90Y. Ammonium acetate buffer (0.5 M) was assocd. with the highest uptake of yttrium. On the basis of kinetic data, the time required to chelate 94% of 90Y (four half-times) under prospective radiopharmacy labeling conditions in 0.5 M ammonium acetate was 17-148 min at pH 6.5, but it was only 1-10 min at pH 7.5. Raising the reaction temp. from 25.degree.C to 37.degree.C markedly increased the chelation rate. Optimal radiolabeling conditions were identified as: 30-min reaction time, 0.5 M ammonium acetate buffer, pH 7-7.5 and 37.degree.C. In eight labeling expts. under optimal conditions, a mean product yield (.+-. s.d.) of 91% .+-. 8% was achieved, comparable to iodination yields. The specific activity of final products was 74-130 MBq (2.0-3.5 mCi) of 90Y per mg of monoclonal antibody. The immunoreactivity of 90Y-labeled immunoconjugates was 100% .+-. 11%. The optimization of 90Y-DOTA chelation conditions represents an important advance in 90Y RIT because it facilitates the dependable and cost-effective prepn. of 90Y-DOTA pharmaceuticals.

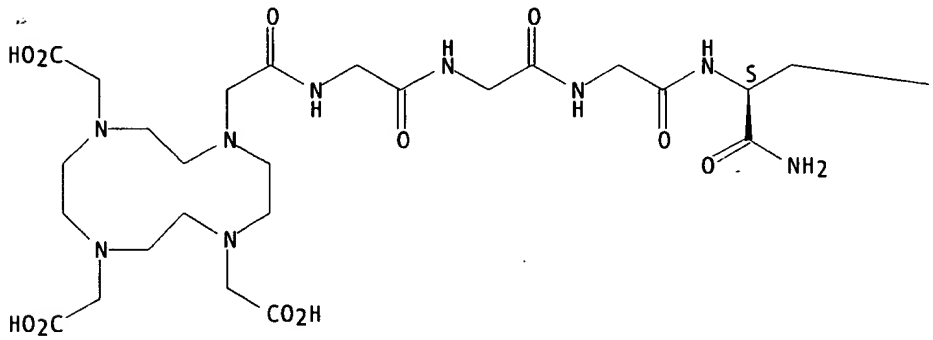
IT **149206-88-2DP**, conjugate with monoclonal antibody
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(optimized conditions for chelation of yttrium-90-DOTA immunoconjugates)

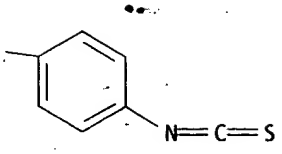
RN 149206-88-2 CAPLUS

CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 33
REFERENCE(S):
(1) Ali, M; Bioconjug Chem 1996, V7, P576 CAPLUS
(2) Beaumier, P; J Nucl Med 1986, V27, P824 CAPLUS
(4) Chakrabarti, M; J Nucl Med 1996, V37, P1384 CAPLUS
(5) Coursey, B; Nucl Med Biol 1993, V20, P693 CAPLUS
(6) DeNardo, G; Antibody Immunoconj Radiopharm 1995, V8, P1 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 25 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:721606 CAPLUS
DOCUMENT NUMBER: 130:7446
TITLE: Stents with a radioactive surface coating, their production and use for restenosis prevention
INVENTOR(S): Dinkelborg, Ludger; Blume, Friedhelm; Hilger, Christoph-Stephan; Heldmann, Dieter; Platzek, Johannes; Niedballa, Ulrich; Miklautz, Heribert; Speck, Ulrich; Duda, Stephan; Tepe, Gunnar; Noll, Bernhard; Goerner, Heidemarie
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848851	A2	19981105	WO 1998-EP2527	19980429
WO 9848851	A3	19990422		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19724230	C1	19981126	DE 1997-19724230	19970603
DE 19724223	C1	19981224	DE 1997-19724223	19970603
DE 19724229	C1	19990401	DE 1997-19724229	19970603
AU 9879100	A1	19981124	AU 1998-79100	19980429
EP 979108	A2	20000216	EP 1998-929272	19980429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 9905310	A	19991029	NO 1999-5310	19991029
PRIORITY APPLN. INFO.:			DE 1997-19718340	19970430
			DE 1997-19718341	19970430
			DE 1997-19718342	19970430
			DE 1997-19724223	19970603
			DE 1997-19724229	19970603
			DE 1997-19724230	19970603
			WO 1998-EP2527	19980429

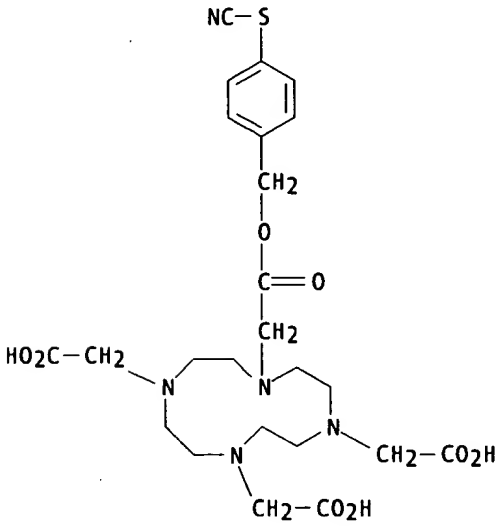
AB The surface of a metallic stent is coated with a radioactive metal isotope by chem. deposition (redn. or pptn.) or electrodeposition, or by chelation with a compd. which adheres to the stent (e.g. a peptide or lipid). Alternatively, the stent may be coated electrochem. with Au and then with a SH group-contg. chelate of a radioactive metal, where the SH group-contg. complexing agent adheres to the Au coating. Thus, a Wiktor stent was immersed in 1 mL EtOH soln. of 1-[3-[N-(2-

methoxyethyl)octadecylsulfamoyl]-2-hydroxypropyl]-4,7,10-tris(hydroxycarbonylmethyl)-1,4,7,10-tetraazacyclododecane, 2 mL H2O was added, and the stent was sonicated for 15 min, removed, and dried. The coated stent was then immersed in 2 mL 0.9% NaCl soln., 37 MBq 111InCl3 was added, and the stent was sonicated for 15 min, rinsed in NaCl soln., and dried. The labeled stent had an activity of 1.49 MBq 111In.

IT 215604-06-1
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stents with radioactive surface coating for restenosis prevention)

RN 215604-06-1 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, mono[(4-thiocyanatophenyl)methyl] ester (9CI) (CA INDEX NAME)



L10 ANSWER 26 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:721605 CAPLUS

DOCUMENT NUMBER: 130:19924

TITLE: Ion pairs, method for the production and use thereof as contrast agents

INVENTOR(S): Krause, Werner; Bauer, Michael; Platzek, Johannes

PATENT ASSIGNEE(S): Schering A.-G., Germany

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848844	A2	19981105	WO 1998-EP2031	19980409
WO 9848844	A3	19990211		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19719033	C1	19990128	DE 1997-19719033	19970429
AU 9876418	A1	19981124	AU 1998-76418	19980409
PRIORITY APPLN. INFO.:			DE 1997-19719033	19970429
			WO 1998-EP2031	19980409

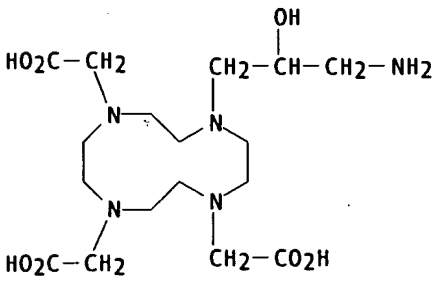
AB The invention relates to novel ion pairs comprising cationic complexes of Bi, Hf and rare earth metals with such ligands as 10-(3-amino-2-hydroxypropyl)-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acids and related ligands and anionic complexes of transition metals and rare earth

metals with such ligands as DTPA, triethylenetetraminehexaacetic acid, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid and related ligands, and their use as contrast agents.

IT 146270-94-2
RL: RCT (Reactant)
(for prepn. of transition metal and rare earth and bismuth polyaminocarboxylate/tetraazacyclododecanepolyacetate complex ion pairs as diagnostic and MRI contrast agents)

RN 146270-94-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



L10 ANSWER 27 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:392724 CAPLUS

DOCUMENT NUMBER: 129:41421

TITLE: Synthesis of macrocyclic metal complex carboxylic acids for use as high-molecular-weight imaging agents for MRI procedures

INVENTOR(S): Platzek, Johannes; Schmitt-Willich, Heribert; Raduechel, Bernd

PATENT ASSIGNEE(S): Schering A.-G., Germany

SOURCE: Ger. Offen., 34 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

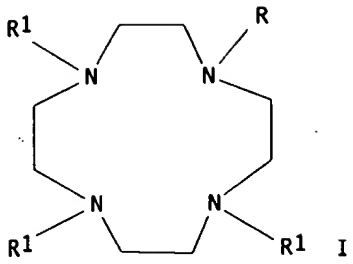
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19652387	A1	19980610	DE 1996-19652387	19961204
WO 9824774	A1	19980611	WO 1997-EP6593	19971126
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9856554	A1	19980629	AU 1998-56554	19971126
EP 946526	A1	19991006	EP 1997-952805	19971126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1239958	A	19991229	CN 1997-180330	19971126

PRIORITY APPLN. INFO.: DE 1996-19652387 19961204
WO 1997-EP6593 19971126

OTHER SOURCE(S): MARPAT 129:41421

GI



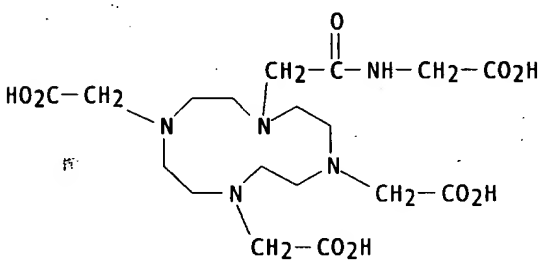
I

AB Title compds. [(I); R = CHXCONHCHY(CH2)xCO2H; X, Y = (independently) H, alkyl, Ph, CH2Ph; x = 0-9; R1 = CH2CO2A; A = H, metal of at. no. 58-71] were synthesized by coupling an amide (prepn. given) to a core structure, and reacting with a metal with the help of a complexing agent. Dendritic polymer forms of the compds. were synthesized to give the high-mol.-wt. desired for MRI imaging contrast materials. Thus, N-(2-bromo-propionyl)glycine benzyl ester was prepd., and reacted with 1, 4, 7, 10-tetraaza-cyclo-dodecane to give I(R = CH(CH3)CONHCOOCH2Ph; R1 = H), which was reacted with BrCH2COOC(CH3)3, and deprotected to give I(R = CH(CH3)CONHCH2CO2H; R1 = CH2CO2H); this compd. reacted with Gd2O3 to give the title complex I[R = CH(CH3)CONHCH2CO2; R1 = CH2CO2--1/3GD3+(II)]. II was conjugated with a variety of NH2-bearing dendritic cores. In in-vivo tests in rats as an extracellular imaging material, II showed less diffusion into intercellular spaces than a comparison agent, with no clearing by the kidneys; in tests in guinea pig lymph tests, II injected s.c. into a hind foot (10.mu.M/kg)showed 30 min. post-injection concns. (in popliteal lymph nodes) of 921.mu.M/l, decreasing to 24 h post-injection concn. (in inguinal nodes) of 13.mu.M/l.

IT **208253-06-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of macrocyclic metal complex carboxylic acids for use as high-mol.-wt. imaging agents for MRI procedures)

RN 208253-06-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(carboxymethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 28 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:388796 CAPLUS

DOCUMENT NUMBER: 129:41420

TITLE: Procedure for production of metal complex-carboxylic acid amides for use as contrast materials for MRI procedures

INVENTOR(S): Schmitt-Willich, Heribert; Platzek, Johannes; Graske, Klaus-Dieter; Raduechel, Bernd

PATENT ASSIGNEE(S): Schering A.-G., Germany

SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

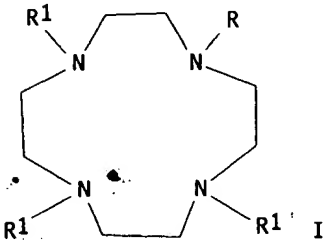
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19652386	A1	19980610	DE 1996-19652386	19961204
WO 9824775	A1	19980611	WO 1997-EP6594	19971126
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9855566	A1	19980629	AU 1998-55566	19971126
EP 946525	A1	19991006	EP 1997-951981	19971126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
ZA 9710930	A	19980908	ZA 1997-10930	19971204
NO 9902710	A	19990603	NO 1999-2710	19990603
PRIORITY APPLN. INFO.:			DE 1996-19652386	19961204
			WO 1997-EP6594	19971126

OTHER SOURCE(S): CASREACT 129:41420; MARPAT 129:41420

GI



I

AB Title compds. [(I); R = CHXCONHCHY(CH2)xCO2H; X, Y = (independently) H, alkyl, Ph, CH2PH; x = 0-9; R1 = CH2CO2A; A = H, metal of at. no. 25, 26, 39, 57-71, 83;] were synthesized by coupling an amine, with the help of a solubilizing agent, in a condensation reaction and with a metal with the help of a complexing agent. By using a salt-formation step with the complex and LiCl or NaBr in DMSO with the coupling reagent, the resulting complex was isolated in good yield. Thus, N-(2-bromo-propionyl)glycine benzyl ester was prepd., and reacted with 1,4,7,10-tetraaza-cyclo-dodecane to give I (R = CH(CH3)CONHCH2COOCH2Ph; R1 = H), which was reacted with BrCH2COOC(CH3)3, and deprotected to give I(R = CH(CH3)CONHCH2CO2H; R1 = CH2CO2H); this compd. reacted with Gd2O3 to give the title complex I[R = CH(CH3)CONHCH2CO2H; R1 = CH2CO2--1/3Gd3+(II)]. II was conjugated with a variety of NH2-bearing compds., including dendritic poly-amines, polylysine, antibiotics, and carbohydrates.

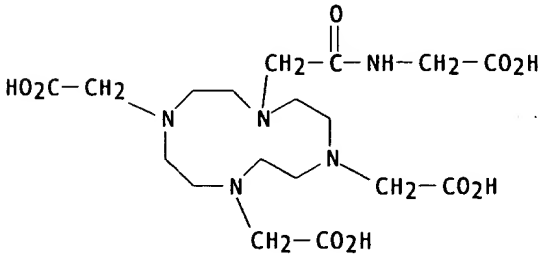
IT **208253-06-9P**

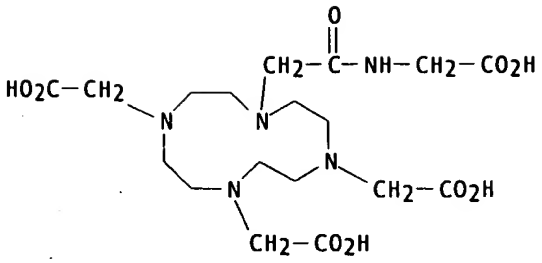
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(procedure for prodn. of metal complex-carboxylic acid amides for use as contrast materials for MRI procedures)

RN 208253-06-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(carboxymethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)





L10 ANSWER 29 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:208521 CAPLUS
DOCUMENT NUMBER: 128:280376
TITLE: Ion pairs, process for producing the same and their use as contrast agents
INVENTOR(S): Krause, Werner; Bauer, Michael
PATENT ASSIGNEE(S): Schering A.-G., Germany; Krause, Werner; Bauer, Michael
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

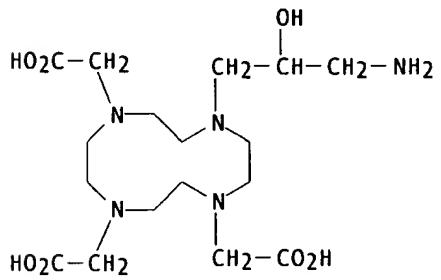
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9813338	A1	19980402	WO 1997-EP5247	19970924
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19641197	A1	19980514	DE 1996-19641197	19960924
DE 19641197	C2	19990218		
AU 9747779	A1	19980417	AU 1997-47779	19970924
PRIORITY APPLN. INFO.:			DE 1996-19641197	19960924
			WO 1997-EP5247	19970924

AB A novel type of ion pairs consists of elec. charged metal complexes and halogenated compds. with an opposite elec. charge. Also disclosed is the prodn. of such ion pairs and their use in diagnosis and therapy.

IT 146270-94-2DP, metal complexes, salts
RL: PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(ion pairs for use as contrast agents)

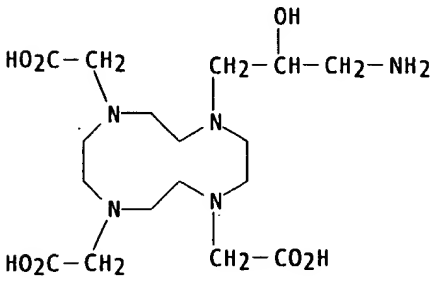
RN 146270-94-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



IT 146270-94-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(ion pairs for use as contrast agents)

RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



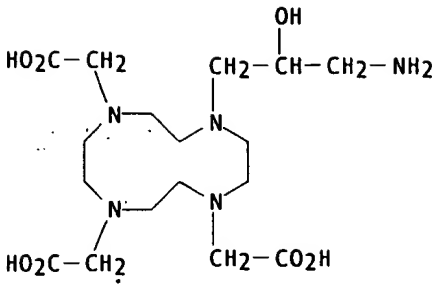
L10 ANSWER 30 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:59193 CAPLUS
DOCUMENT NUMBER: 128:129401
TITLE: Pseudopolyrotaxanes containing metal complexes or iodine
INVENTOR(S): Platzek, Johannes; Schmitt-Willich, Heribert
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19629494	A1	19980115	DE 1996-19629494	19960709
WO 9801163	A2	19980115	WO 1997-EP3344	19970625
WO 9801163	A3	19980409		
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9733446	A1	19980202	AU 1997-33446	19970625
EP 917474	A2	19990526	EP 1997-929292	19970625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000514850	T2	20001107	JP 1998-504710	19970625
PRIORITY APPLN. INFO.:			DE 1996-19629494	19960709
			WO 1997-EP3344	19970625

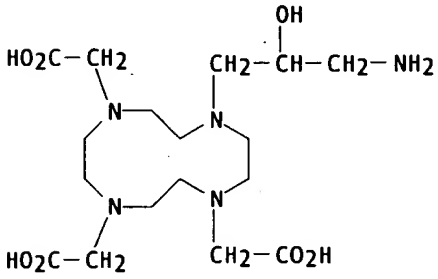
AB The title materials, useful for MRI or x-ray diagnostics or pharmaceuticals, are based on cyclodextrin derivs. contg. metal complexes or I and polyalkylene glycols or arom. or cycloaliph. amides. A typical metal complex was manufd. by reacting 1.26 g 6,6',6'',6''',6'''',6'''''-hexamino-6,6',6'',6''',6'''',6'''''-hexadeoxy-.alpha.-cyclodextrin hexahydrochloride with 7.26 g N3-(2,6-dioxomorpholinoethyl)-N6-(ethoxycarbonylmethyl)-3,6-diazaoctanedicarboxylic acid in water at pH 7.5-8, adjusting the pH to >13 with NaOH, stirring 3 h, treating the basic soln. with Amberlite IR to adjust the pH to 5, filtering-off the ion exchanger, and stirring 30 min at 80.degree. with 4.75 g GdCl3 at pH 7.2.

IT 146270-94-2DP, gadolinium complexes 146270-94-2P 174700-60-8P 174700-61-9DP, gadolinium complexes 174700-62-0DP, gadolinium complexes 174700-63-1DP, gadolinium complexes contg, alanylcyclodextrin thioureas
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation)
(precursor; pseudopolyrotaxanes contg. metal complexes or iodine for pharmaceuticals and diagnostic agents)

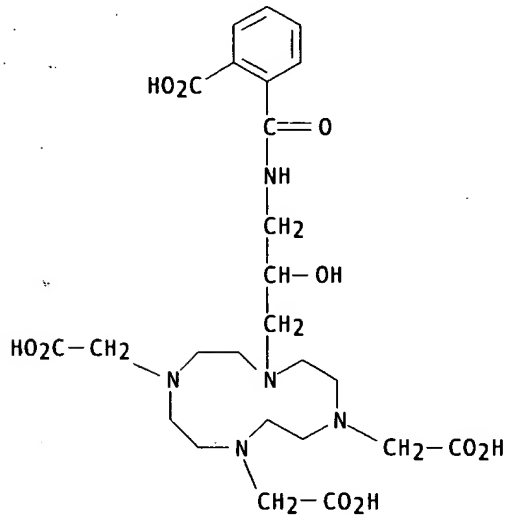
RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)

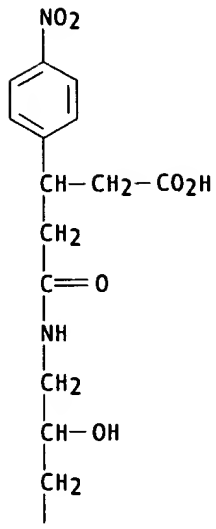


RN 174700-60-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(2-carboxybenzoyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

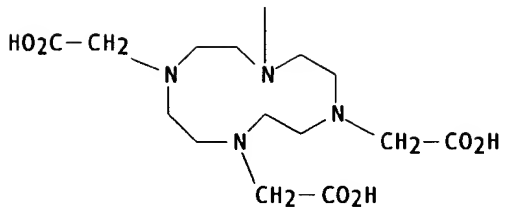


RN 174700-61-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-nitrophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

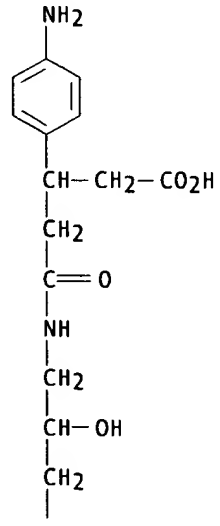


PAGE 2-A

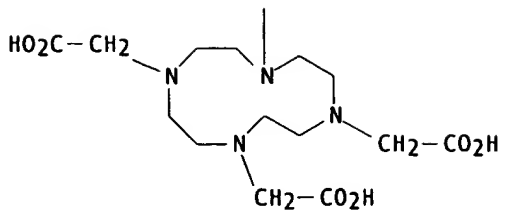


RN 174700-62-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[3-(4-aminophenyl)-4-carboxy-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

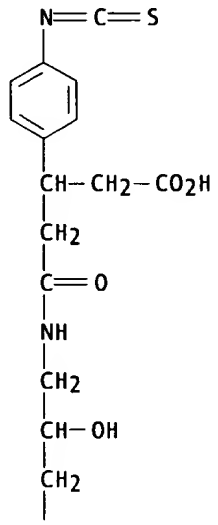


PAGE 2-A

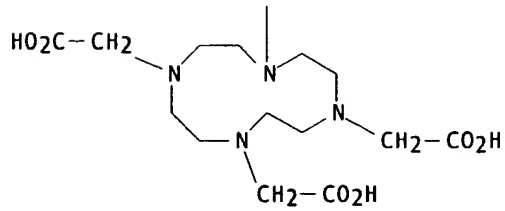


RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

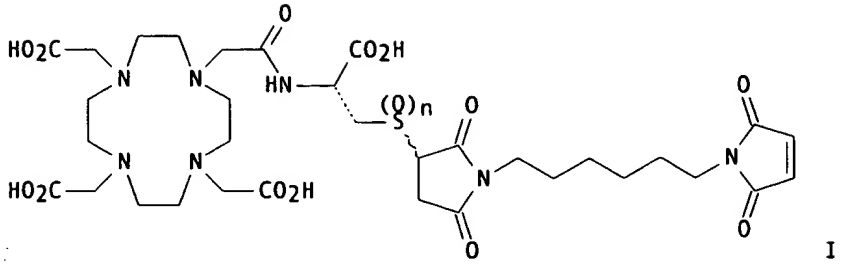


PAGE 2-A



L10 ANSWER 31 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:76 CAPLUS
DOCUMENT NUMBER: 128:61772
TITLE: Maleimidocysteineamido-DOTA Derivatives: New Reagents for Radiometal Chelate Conjugation to Antibody Sulfhydryl Groups Undergo pH-Dependent Cleavage Reactions
AUTHOR(S): Lewis, Michael R.; Shively, John E.
CORPORATE SOURCE: City of Hope Graduate Program in Biological Sciences,

Duarte, CA, 91010, USA
SOURCE: Bioconjugate Chem. (1998), 9(1), 72-86
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

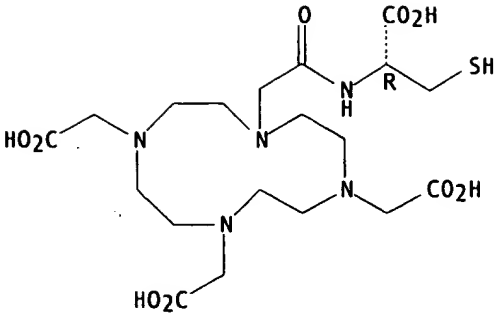
AB Two bifunctional derivs. I (n = 0, 2) of the macrocyclic chelating agent 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA) equipped with maleimide groups for conjugation to reduced disulfide bonds of monoclonal antibodies were prepd. Using water-sol. carbodiimide chem., DOTA was coupled to L-cysteine to incorporate both a "pendent-type" carboxyl group for metal coordination and an orthogonal thiol group for protein attachment. The homobifunctional reagent 1,6-bis(maleimido)hexane was then used to introduce the maleimide functionality via a sulfide linkage to the macrocycle, and alternatively, the sulfide group was converted to a sulfone side chain. Both maleimide derivs. I were conjugated to the anticarcinoembryonic antigen chimeric monoclonal antibody cT84.66 after light redn. of the mAb with dithiothreitol. In this manner, antibody conjugates were prepd. which afforded near-quant. labeling with the radiometals 111In(III) and 90Y(III) as well as quant. immunoreactivity. Radioimmunoconjugates prepd. with the sulfide and sulfone compds. exhibited relatively rapid linker-dependent radiometal loss when incubated in human serum and aq. solns. at physiol. temp. and pH. The unconjugated maleimidocysteineamido-DOTA derivs. and their Y(III) complexes were incubated in aq. soln. at 37.degree., and the resulting decompn. products were analyzed by HPLC and mass spectrometry. These studies revealed that the two bifunctional chelating agents underwent linker-specific cleavage reactions which were considerably faster at pH 7.4 than at pH 5.4. The chem. labile linker systems are expected to release chelated radiometal from mAb conjugates in a pH-dependent manner. This property may impart favorable tumor uptake and normal tissue clearance on radioimmunoconjugates prepd. with these reagents, on the basis of the observation that many solid tumors are significantly more acidic than normal tissues.

IT **200402-61-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and pH-dependent cleavage of maleimidocysteineamido-DOTA derivs. as new reagents for radiometal chelate conjugation to antibody sulfhydryl groups)

RN 200402-61-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(1-carboxy-2-mercaptoethyl)amino]-2-oxoethyl]-, (R)- (9CI) (CA INDEX NAME)

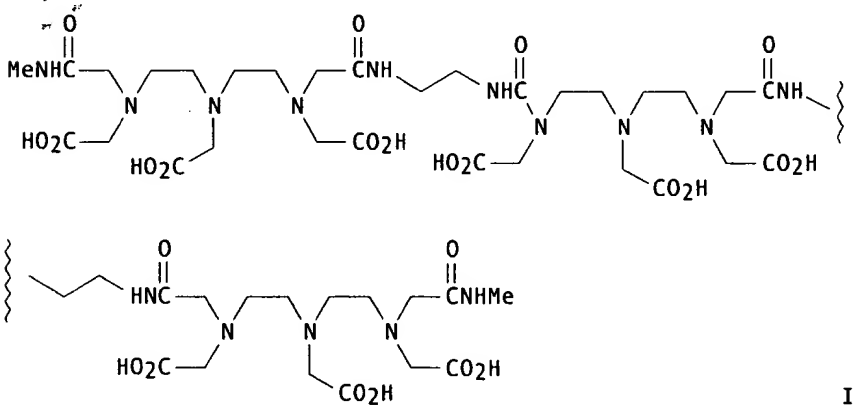
Absolute stereochemistry.



L10 ANSWER 32 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:705846 CAPLUS
DOCUMENT NUMBER: 127:325683
TITLE: Preparation of linear oligomeric polychelant polyaminocarboxylic acids and derivatives and their metal chelates
INVENTOR(S): Love, David B.; Dow, William C.; Himmelsbach, Richard J.; Watson, Alan D.; Rocklage, Scott M.
PATENT ASSIGNEE(S): Salutar, Inc., USA
SOURCE: U.S., 20 pp. Cont.-in-part of U.S. 5,446,146.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5679810	A	19971021	US 1995-480056	19950607
US 5281704	A	19940125	US 1990-468107	19900119
JP 2000136174	A2	20000516	JP 1999-192219	19901020
US 5446145	A	19950829	US 1993-86996	19930707
PRIORITY APPLN. INFO.:			US 1990-468107	19900119
			US 1993-86996	19930707
			GB 1989-23843	19891023
			JP 1990-515144	19901020

GI



I

AB Disclosed are linear oligomeric polychelants comprising alternating linker and non-conjugated chelant moieties bound together by amide or ester moieties with the carbonyl groups adjacent to the chelant moieties, and their salt or chelate complexes. The compds. have 3-100 chelant moieties, at least one of which complexes a paramagnetic metal ion. Thus, claimed

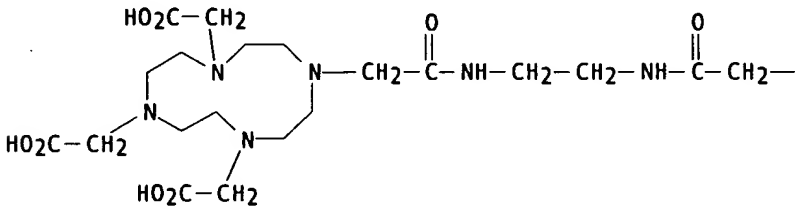
polyaminocarboxylic acid I.cntdot.6H2O is prepd. via an amidation procedure. The claimed gadolinium complex of I.cntdot.6H2O is formed as a homogeneous aq. soln. The prepn. of many other polyaminocarboxylic acids, derivs., and their complexation with Gd, Dy, or Hf are also presented. The polychelants and esp. their paramagnetic metal polychelates are particularly suitable for diagnostic imaging.

IT 137097-99-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of linear oligomeric polychelant polyaminocarboxylic acids and their paramagnetic metal chelates for diagnostic imaging)

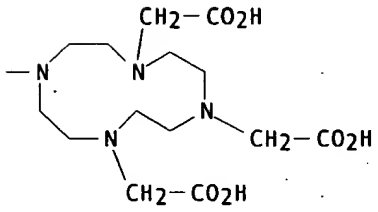
RN 137097-99-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[imino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L10 ANSWER 33 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1997:579696 CAPLUS

DOCUMENT NUMBER: 127:228839

TITLE: Pharmaceutical agents containing perfluoroalkyl-containing metal complexes and the use thereof in tumor therapy and intervention al radiology

INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduchel, Bernd; Schlecker, Wolfgang; Weinmann, Hanns-Joachim; Frenzel, Thomas

PATENT ASSIGNEE(S): Schering A.-G., Germany

SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9730969	A1	19970828	WO 1997-EP684	19970214
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19608278	A1	19970828	DE 1996-19608278	19960223
CA 2247253	AA	19970828	CA 1997-2247253	19970214
AU 9717692	A1	19970910	AU 1997-17692	19970214
EP 882010	A1	19981209	EP 1997-903278	19970214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

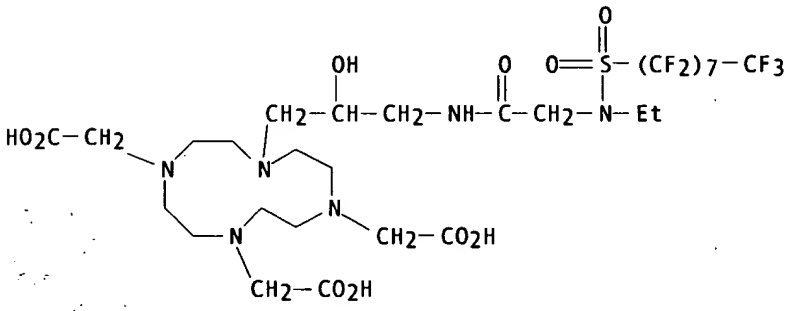
JP 2000504736	T2	20000418	JP 1997-529766	19970214
US 6180113	B1	20010130	US 1997-801983	19970219
NO 9803875	A	19981022	NO 1998-3875	19980821
PRIORITY APPLN. INFO.:			DE 1996-19608278	19960223
			US 1996-12506	19960229
			WO 1997-EP684	19970214

OTHER SOURCE(S): MARPAT 127:228839

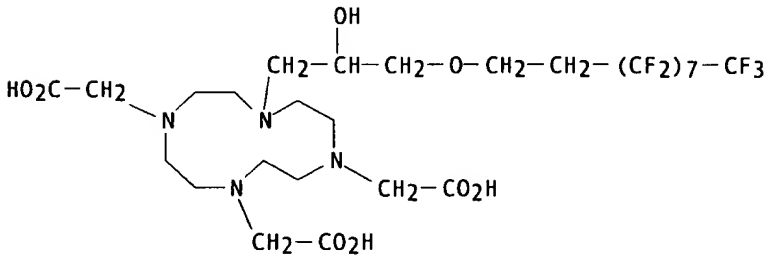
AB The invention relates to pharmaceutical agents contg. perfluoro alkylated metal complexes RF-L-A and the use thereof in tumor therapy and interventional radiol., in which formula RF is a perfluorinated, straight-chain or branched C chain with the formula -CnF2nX (X = terminal F, Cl, Br, I or H atom and n = 4-30), L is a binding group, and A is a metal complex or the salts thereof of org. and/or inorg. bases or amino acids or amino acid amides. Thus Gd/Dy/Y/Mn complexes of tetraazacyclododecane having amide pendants with perfluoroalkyl groups or polyaminopolycarboxylic acids with pendants contg. perfluoroalkyl groups were prepd.

IT **193528-82-4P 193528-87-9P 193528-89-1P**
193528-92-6P 193528-98-2P 193529-08-7P
193529-11-2P 193529-15-6P 195046-92-5P
195046-94-7P 195047-05-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of rare earth/manganese fluoroalkyl-contg. polyaminopolycarboxylate/tetraazacyclododecane complexes for use as pharmaceutical agents in tumor therapy and interventional radiol.)

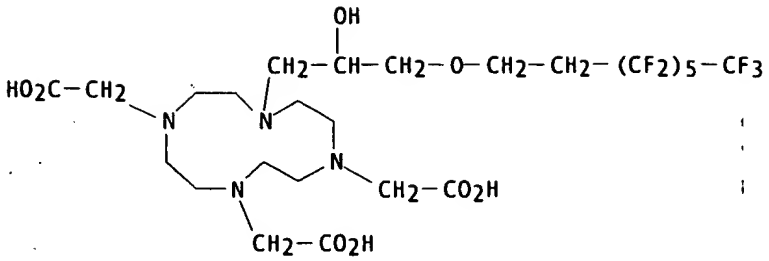
RN 193528-82-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[[ethyl[(heptadecafluorooctyl)sulfonyl]amino]acetyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



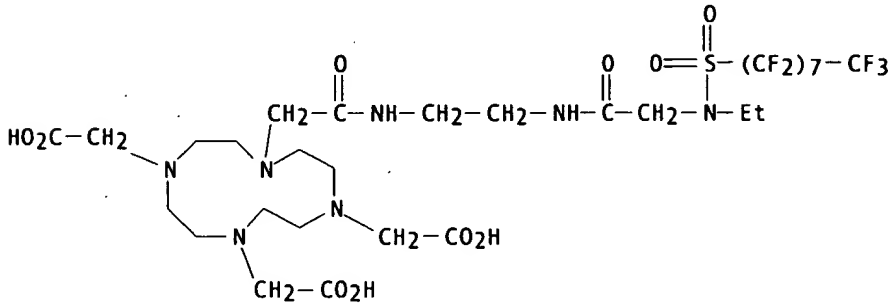
RN 193528-87-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)oxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



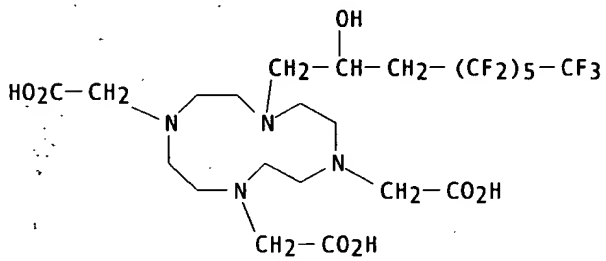
RN 193528-89-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)oxy]propyl]- (9CI) (CA INDEX NAME)



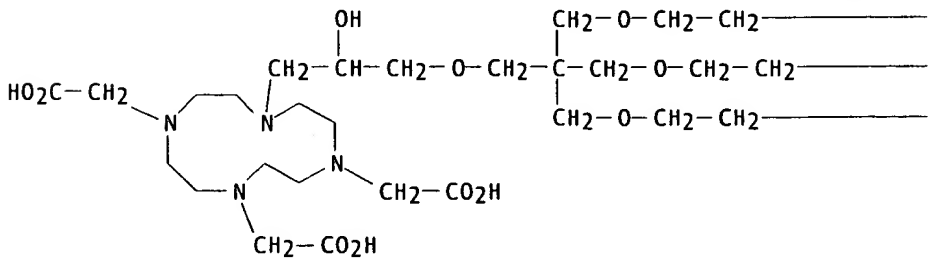
RN 193528-92-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(9-ethyl-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-10,10-dioxido-2,7-dioxo-10-thia-3,6,9-triazaoctadec-1-yl)- (9CI) (CA INDEX NAME)



RN 193528-98-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-hydroxynonyl)- (9CI) (CA INDEX NAME)



RN 193529-08-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[3-[(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)oxy]-2,2-bis[[(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)oxy]methyl]propoxy]propyl]- (9CI) (CA INDEX NAME)



PAGE 1-B

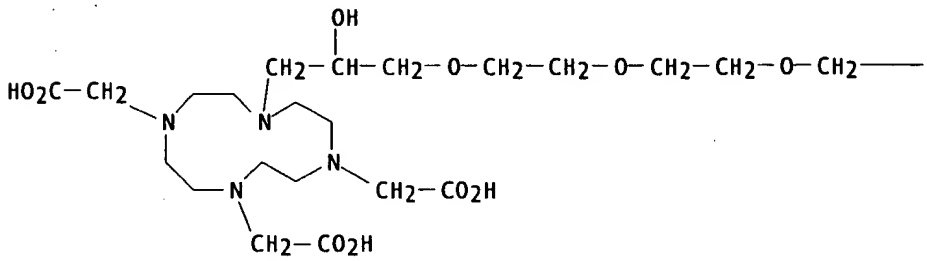
$-(CF_2)_5-CF_3$

$-(CF_2)_5-CF_3$

$-(CF_2)_5-CF_3$

RN 193529-11-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(19,19,20,20,21,21,22,22,23,23,24,24,25,25,26,26,26-heptadecafluoro-2-hydroxy-4,7,10,13,16-pentaoxahexacos-1-yl)- (9CI) (CA INDEX NAME)

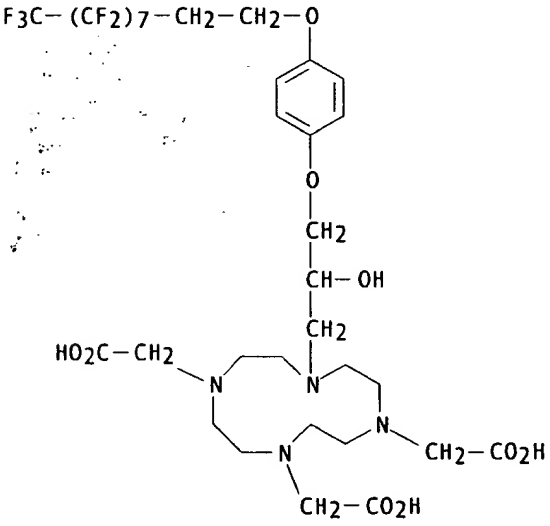
PAGE 1-A



PAGE 1-B

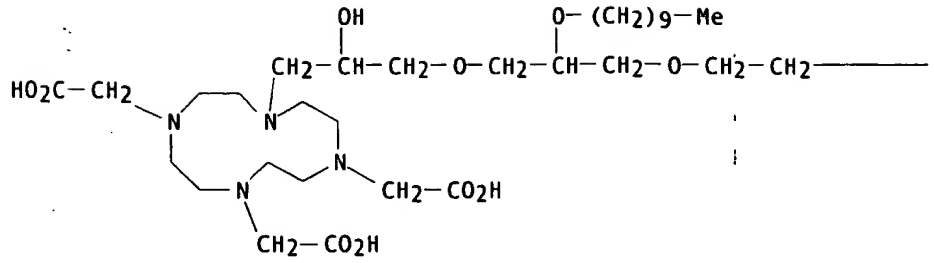
$-CH_2-O-CH_2-CH_2-O-CH_2-CH_2-(CF_2)_7-CF_3$

RN 193529-15-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)oxy]phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 195046-92-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[2-(decyloxy)-3-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)oxy]propoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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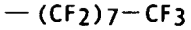

RN 195046-94-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[15-ethyl-9-[2-[[[ethyl[(heptadecafluorooctyl)sulfonyl]amino]acetyl]amino]ethyl]-17,17,18,18,19,19,20,20,21,21,22,22,23,23,24,24,24-heptadecafluoro-2-hydroxy-16,16-dioxido-5,8,13-trioxo-16-thia-4,9,12,15-tetraazatetracos-1-yl]- (9CI) (CA INDEX NAME)

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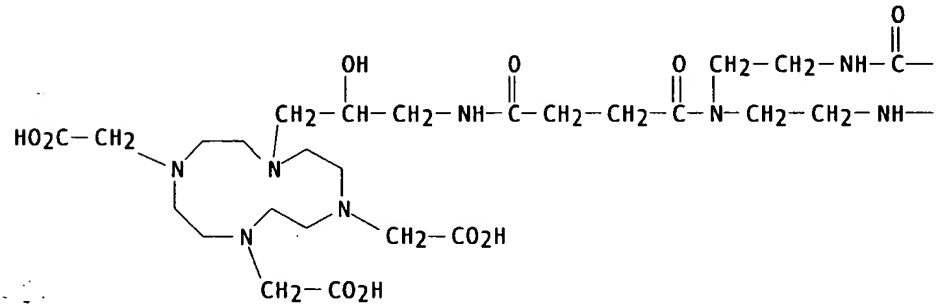

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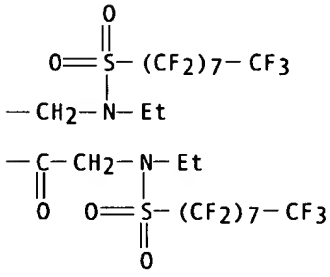
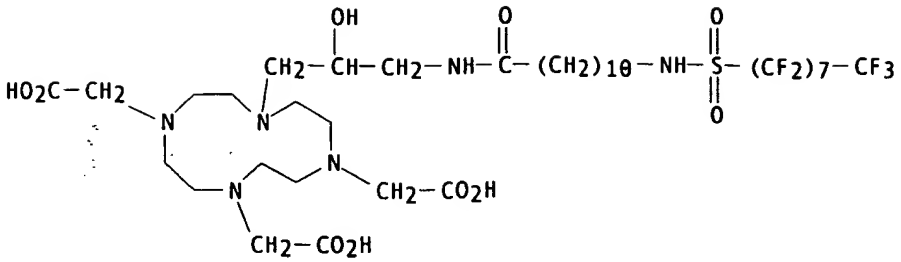


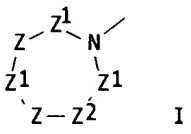
RN 195047-05-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[11-[[(heptadecafluorooctyl)sulfonyl]amino]-1-oxoundecyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 34 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:527643 CAPLUS
DOCUMENT NUMBER: 127:190761
TITLE: Preparation of amide-linked bis(DOTA) compounds as contrast agent chelants
INVENTOR(S): Carvalho, Joan; Watson, Alan D.; Fellmann, Jere D.; Koo, Michael David
PATENT ASSIGNEE(S): Nycomed Salutar, USA
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. Ser. No. 855,028, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5650133	A	19970722	US 1994-226760	19940412
US 5281704	A	19940125	US 1990-468107	19900119
JP 2000136174	A2	20000516	JP 1999-192219	19901020
US 5446145	A	19950829	US 1993-86996	19930707
CA 2172735	AA	19950413	CA 1994-2172735	19940929
CN 1136313	A	19961120	CN 1994-194300	19940929
CN 1045772	B	19991020		
HU 74592	A2	19970128	HU 1996-805	19940929
US 5972307	A	19991026	US 1997-898376	19970722
PRIORITY APPLN. INFO.:			US 1990-468107	19900119
			US 1992-855028	19920612
			US 1993-86996	19930707
			GB 1993-20277	19931001
			GB 1989-23843	19891023
			JP 1990-515144	19901020
			US 1992-885028	19920612
			US 1994-226760	19940412

OTHER SOURCE(S): MARPAT 127:190761
GI



I

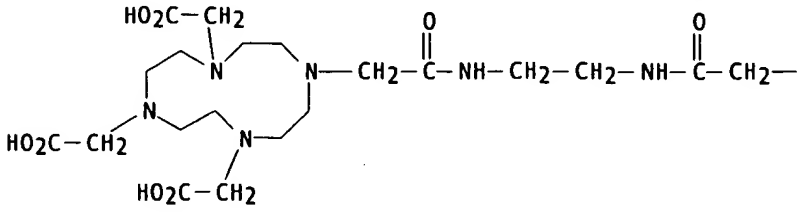
AB [R(CH2)q]2Z3 [R = polyaza macrocyclic group I; .gtoreq.2 of Z = NR2 and the others = NR2, O, S; R2 = R1 or CR12R3; R1 = H, (hydroxy)alkyl, alkoxyalkyl; R3 = CO2H, SO3H, PO3H, etc.; Z1 = (CR12)2-3; Z2 = (Z1Z)m; Z3 = bridging group; m = 0-2; q = 1 or 2] and Gd complexes thereof were prepd. Thus, (CH2NHMe)2 was bisalkylated by BrCH2COBr and the product bisamidated by RH [R = I, Z = NCH2CO2R4, Z1 = CH2CH2, Z2 = CH2CH2N(CH2CO2R4)](II; R4 = CMe3)(prepn. given) to give, after deprotection, (CH2NMeCH2COR)2 (R = II, R4 = H).
IT 137097-99-5P 167407-69-4P 167407-72-9P

167407-74-1P 194164-18-6P 194164-25-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of amide-linked bis(DOTA) compds. as contrast agent chelants)

RN 137097-99-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[imino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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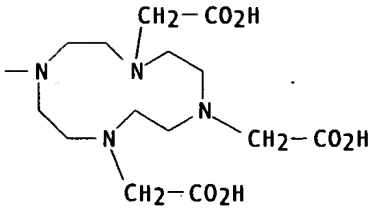
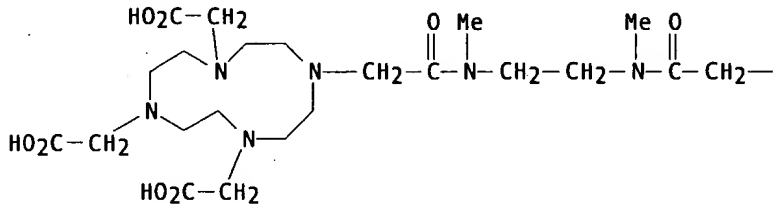


RN 167407-69-4 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[(methylimino)(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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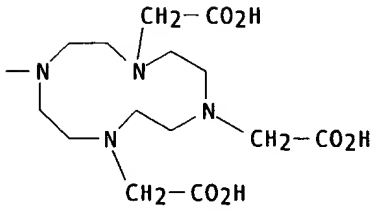
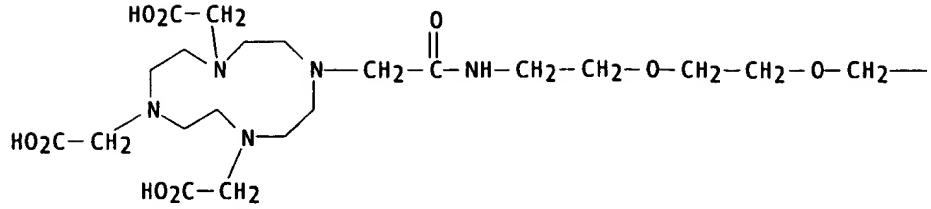


RN 167407-72-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(2,13-dioxo-6,9-dioxa-3,12-diazatetradecane-1,14-diyl)bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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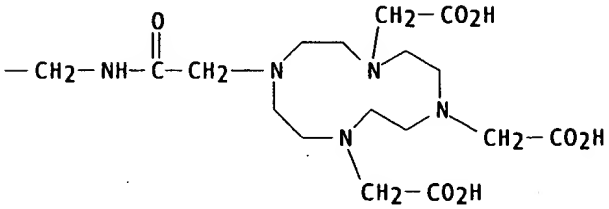
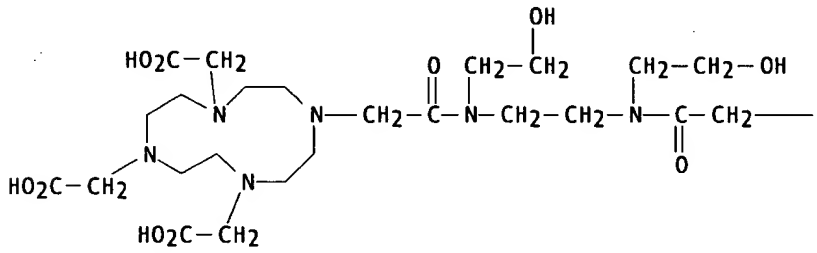


RN 167407-74-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, [1,2-ethanediylbis[[(2-hydroxyethyl)imino](2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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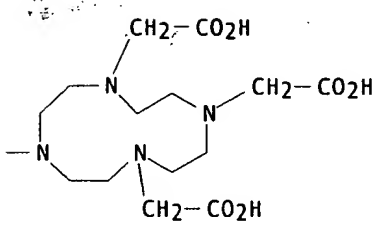
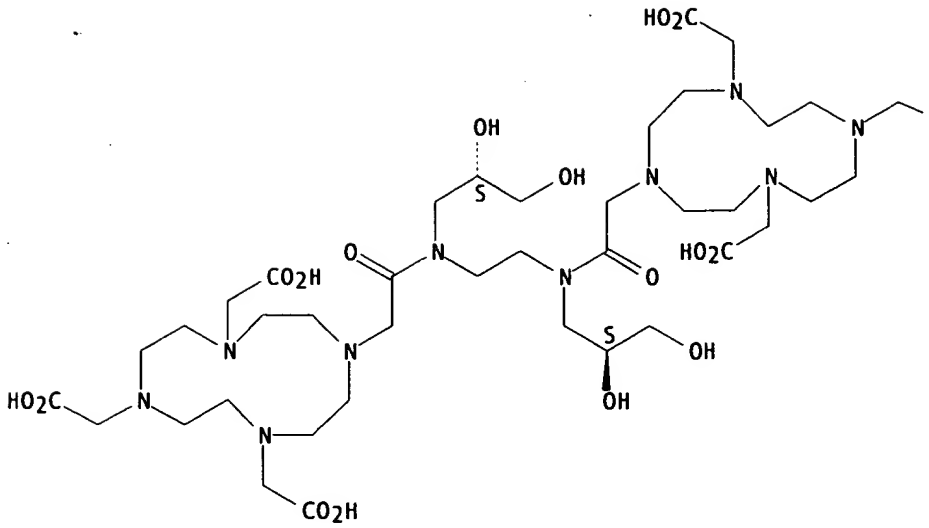


RN 194164-18-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[[(2,3-dihydroxypropyl)imino](2-oxo-2,1-ethanediyl)]]bis-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

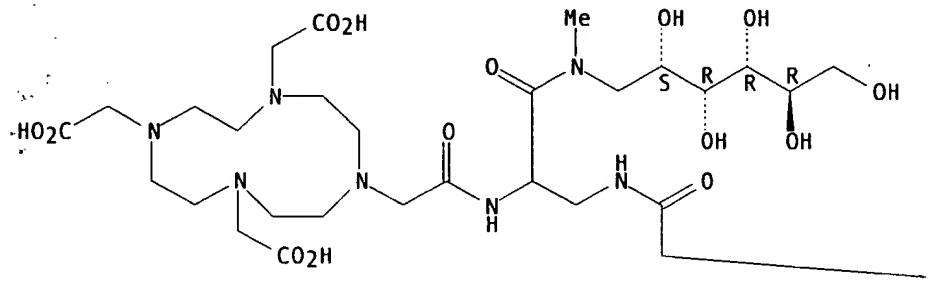


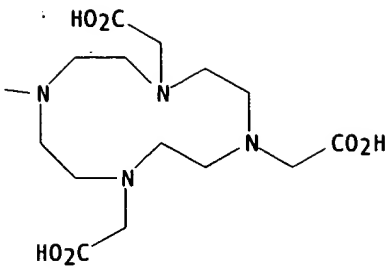
PAGE 1-B

RN 194164-25-5 CAPLUS
CN D-Glucitol, 1-deoxy-1-[methyl[1-oxo-2,3-bis[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]propyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





L10 ANSWER 35 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:499124 CAPLUS
DOCUMENT NUMBER: 127:170662
TITLE: Perfluoroalkyl-containing metal complexes and their use in NMR diagnostics
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduchel, Bernd; Schlecker, Wolfgang; Weinmann, Hanns-joachim; Frenzel, Thomas; Misselwitz, Bernd; Ebert, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9726017	A2	19970724	WO 1997-EP209	19970116
WO 9726017	A3	19971120		
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19603033	A1	19970724	DE 1996-19603033	19960119
CA 2243316	AA	19970724	CA 1997-2243316	19970116
AU 9715977	A1	19970811	AU 1997-15977	19970116
AU 716788	B2	20000309		
EP 874645	A2	19981104	EP 1997-902179	19970116
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CN 1209754	A	19990303	CN 1997-191770	19970116
BR 9707053	A	19990720	BR 1997-7053	19970116
JP 2000506511	T2	20000530	JP 1997-525698	19970116
NO 9803287	A	19980921	NO 1998-3287	19980716
PRIORITY APPLN. INFO.:			DE 1996-19603033	19960119
			WO 1997-EP209	19970116

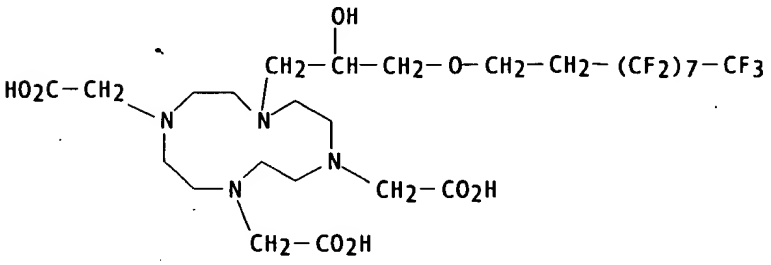
OTHER SOURCE(S): MARPAT 127:170662

AB Gd and other lanthanide and MN complexes of perfluoroalkyl-substituted ligands of tetraazacyclododecane and polyaminoalkanes were prepd. and used in diagnostics and therapy. The compds. according to the invention to the invention are particularly suited for use as in vivo contrast agents in nuclear spin resonance tomog. (MRT). They can be preferably used as blood pool agents and contrast agents for lymphog.

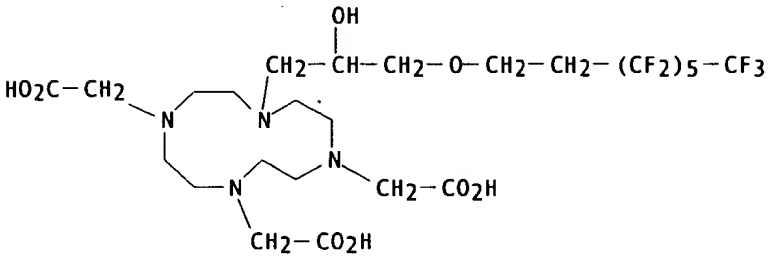
IT 193528-87-9P 193528-89-1P 193528-92-6P
193528-98-2P 193529-06-5P 193529-08-7P
193529-10-1P 193529-11-2P 193529-15-6P

193529-38-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with gadolinium)

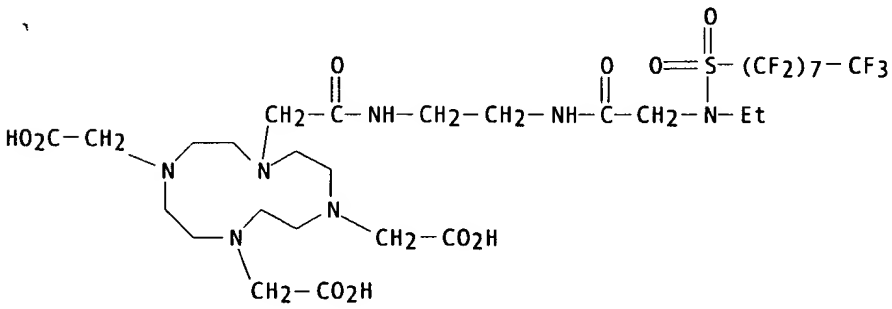
RN 193528-87-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)oxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



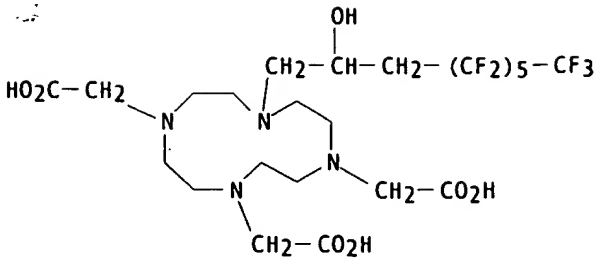
RN 193528-89-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)oxy]propyl]- (9CI) (CA INDEX NAME)



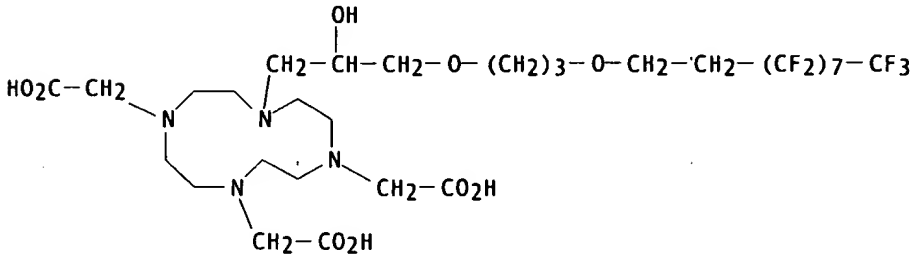
RN 193528-92-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(9-ethyl-11,11,12,12,13,13,14,14,15,15,16,16,17,17,18,18,18-heptadecafluoro-10,10-dioxido-2,7-dioxo-10-thia-3,6,9-triazaoctadec-1-yl)- (9CI) (CA INDEX NAME)



RN 193528-98-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluoro-2-hydroxynonyl)- (9CI) (CA INDEX NAME)

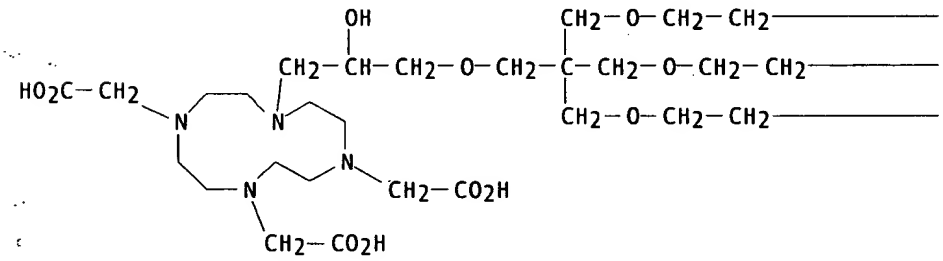


RN 193529-06-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[3-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)oxy]propoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 193529-08-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[3-[(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)oxy]-2,2-bis[[(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)oxy]methyl]propoxy]propyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

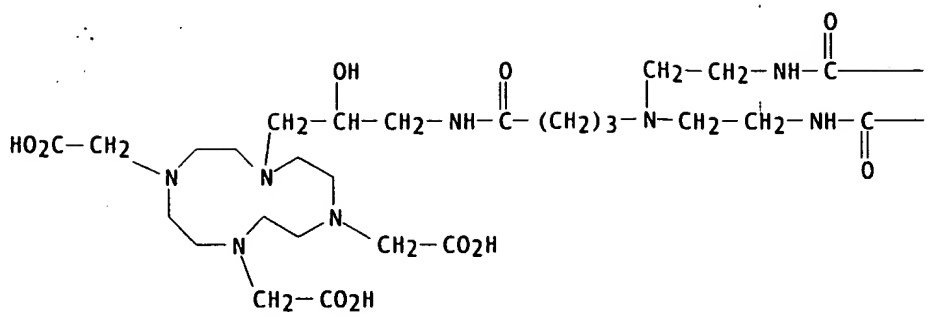
— $(CF_2)_5-CF_3$

—— $(CF_2)_5-CF_3$

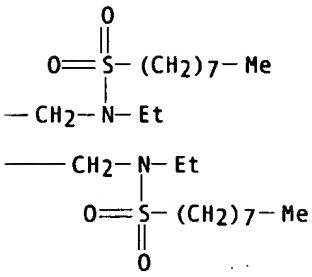
— $(CF_2)_5-CF_3$

RN 193529-10-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[15-ethyl-9-[2-[[[ethyl(octylsulfonyl)amino]acetyl]amino]ethyl]-2-hydroxy-16,16-dioxido-5,13-dioxo-16-thia-4,9,12,15-tetraazatetracos-1-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A

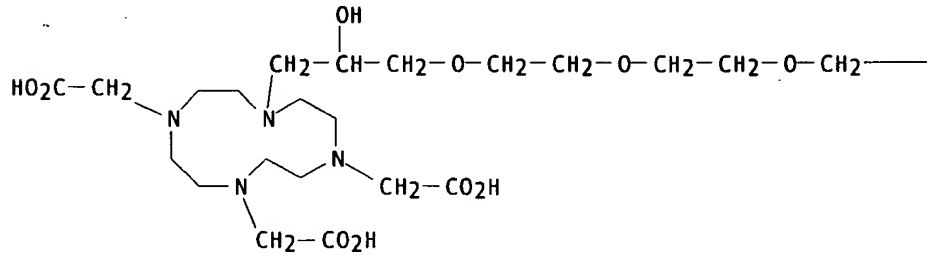


PAGE 1-B

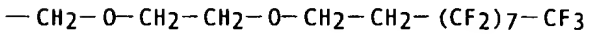


RN 193529-11-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(19,19,20,20,21,21,22,22,23,23,24,24,25,25,26,26,26-heptadecafluoro-2-hydroxy-4,7,10,13,16-pentaoxahexacos-1-yl)- (9CI) (CA INDEX NAME)

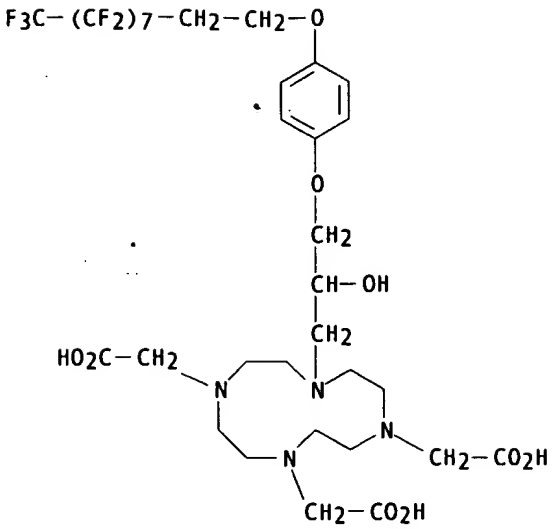
PAGE 1-A



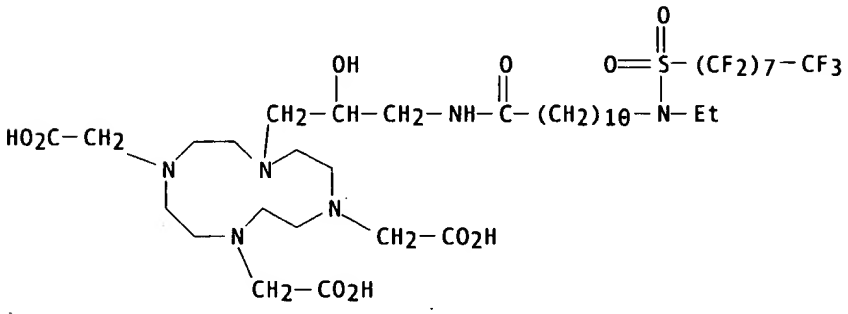
PAGE 1-B



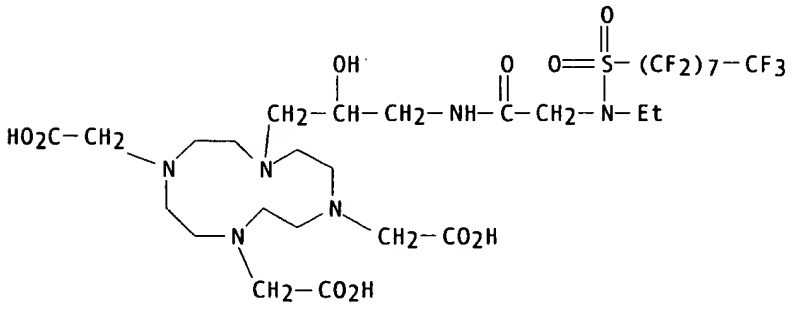
RN 193529-15-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)oxy]phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 193529-38-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[11-[ethyl[(heptadecafluorooctyl)sulfonyl]amino]-1-oxoundecyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



IT 193528-82-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with transition metals)
RN 193528-82-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[[ethyl[(heptadecafluorooctyl)sulfonyl]amino]acetyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



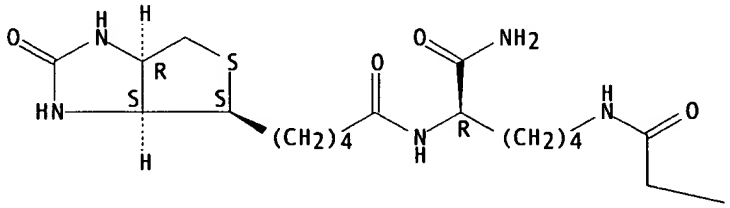
L10 ANSWER 36 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:433657 CAPLUS
DOCUMENT NUMBER: 127:92211
TITLE: Development of a Streptavidin-Anti-Carcinoembryonic Antigen Antibody, Radiolabeled Biotin Pretargeting Method for Radioimmunotherapy of Colorectal Cancer.

Reagent Development

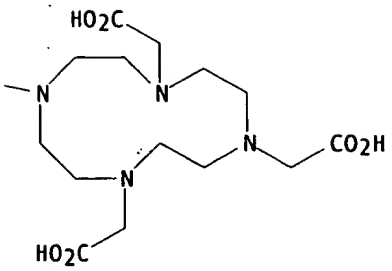
AUTHOR(S): Karacay, Habibe; Sharkey, Robert M.; Govindan, Serengulam V.; McBride, William J.; Goldenberg, David M.; Hansen, Hans J.; Griffiths, Gary L.
CORPORATE SOURCE: Immunomedics Inc., Morris Plains, NJ, 07950, USA
SOURCE: Bioconjugate Chem. (1997), 8(4), 585-594
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB With "pretargeting", radioisotope delivery to tumor is decoupled from the long antibody localization process, and this can increase tumor:blood ratios dramatically. Several reagents were prepd. for each step of a "two-step" pretargeting method, and their properties were investigated. For pretargeting tumor, streptavidin-monoclonal antibody (StAv-mab) conjugates were prepd. by crosslinking sulfo-SMCC-derivatized streptavidin to a free thiol (SH) group on MN-14 [a high-affinity anti-carcinoembryonic antigen (CEA) mab]. Thiolated mabs were generated either by reaction of 2-iminothiolane (2-IT) with mab lysine residues or by redn. of mab disulfide bonds with (2-mercaptoethyl)amine (MEA). Both procedures gave protein-protein conjugates isolated in relatively low yields (20-25%) after preparative size-exclusion (SE) chromatog. purifn. with conservative peak collection. Both StAv-MN-14 conjugates retained their ability to bind to CEA, to an anti-idiotypic antibody to MN-14 (WI2), and to biotin, as demonstrated by SE-HPLC. Two clearing agents, WI2 mab and a biotin-human serum albumin (biotin-HSA) conjugate, were developed to remove excess circulating StAv-MN-14 conjugates in animals. Both clearing proteins were also modified with galactose residues, introduced using an activated thioimidate deriv., to produce clearing agents which would clear rapidly and clear primary mab rapidly. At least 14 galactose residues on WI2 were required to reduce blood levels to 5.9 .+-. 0.7% ID/g in 1 h. Faster blood clearance (0.7 .+-. 0.2% ID/g) was obsd. in 1 h using 44 galactose units per WI2. For the delivery of radioisotope to tumor, several biotinylated conjugates consisting of biotin, a linker, and a chelate were prepd. Conjugates showed good in vitro and in vivo stability when D-amino acid peptides were used as linkers. Biotin-peptide-DOTA-indium-111 had a slightly longer blood circulation time (0.09 .+-. 0.02% ID/g in 1 h) than biotin-peptide-DTPA-indium-111 (0.05 .+-. 0.03% ID/g in 1 h) in nude mice. A longer circulation time with the neutral DOTA complex might allow higher tumor uptake.
IT **192221-17-3P 192221-19-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; streptavidin-anticarcinoembryonic antigen antibody, radiolabeled biotin pretargeting for radioimmunotherapy of colorectal cancer)
RN 192221-17-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(5R)-6-amino-5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



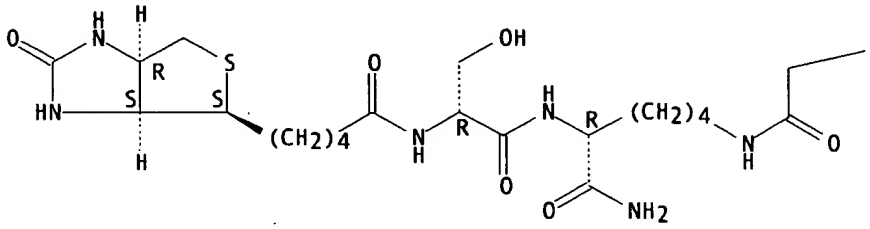
PAGE 1-B



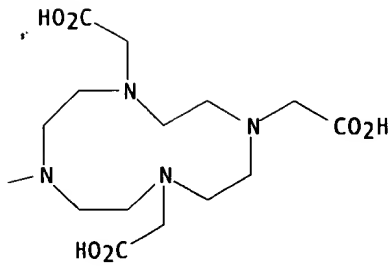
RN 192221-19-5 CAPLUS
CN D-Lysinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-D-seryl-N6-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



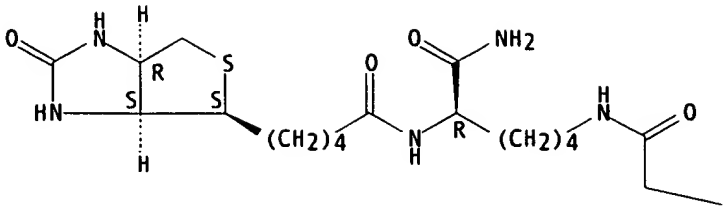
PAGE 1-B



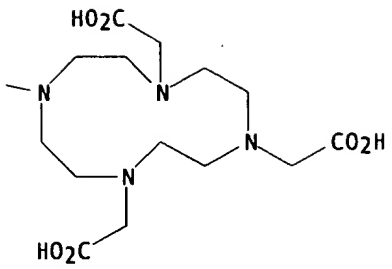
IT 192221-17-3DP, In-111 complexes 192221-19-5DP, In-111 complexes
RL: BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(streptavidin-anticarcinoembryonic antigen antibody, radiolabeled biotin pretargeting for radioimmunotherapy of colorectal cancer)
RN 192221-17-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(5R)-6-amino-5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



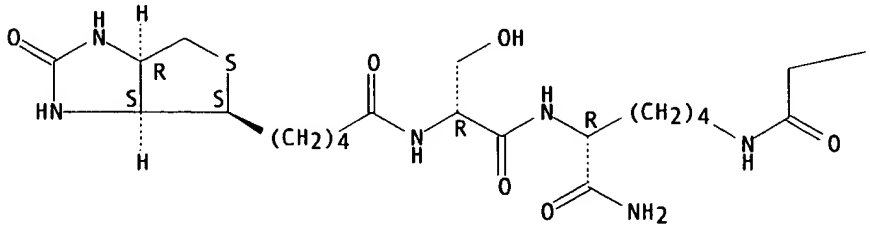
PAGE 1-B

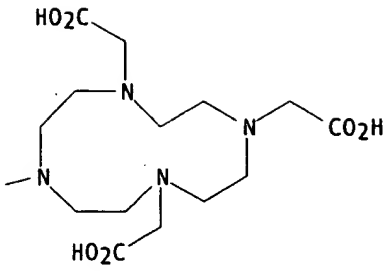


RN 192221-19-5 CAPLUS
CN D-Lysinamide, N-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-D-seryl-N6-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



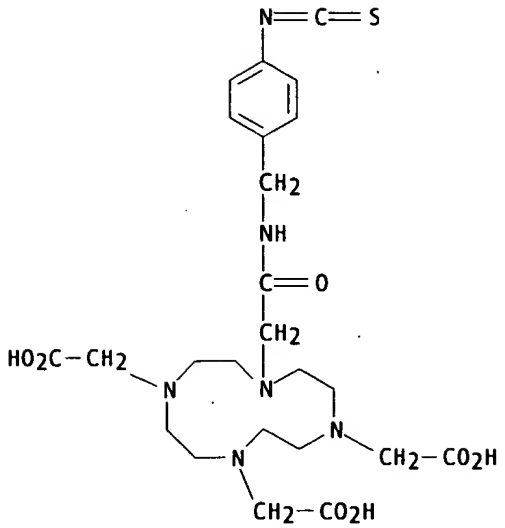


L10 ANSWER 37 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:360531 CAPLUS
DOCUMENT NUMBER: 127:62565
TITLE: Gadolinium(III) DO3A macrocycles and polyethylene glycol coupled to dendrimers. Effect of molecular weight on physical and biological properties of macromolecular magnetic resonance imaging contrast agents
AUTHOR(S): Margerum, Lawrence D.; Campion, Brian K.; Koo, Mike; Shargill, Narinder; Lai, Jan-Ji; Marumoto, Alan; Sontum, Per Christian
CORPORATE SOURCE: Department of Chemistry, University of San Francisco, San Francisco, CA, USA
SOURCE: J. Alloys Compd. (1997), 249(1-2), 185-190
CODEN: JALCEU; ISSN: 0925-8388
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

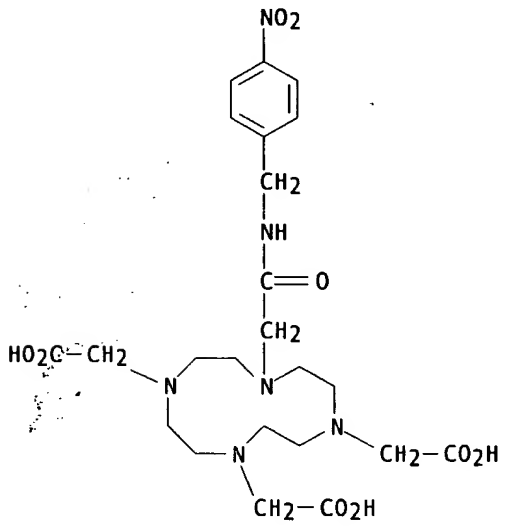
AB The macrocycle 1-(4-isothiocyanatobenzyl)amido-4,7,10-triacetic acid-tetraazacyclododecane (DO3A-bz-NCS) was synthesized and coupled to the terminal amine sites of a series of different generations (Gn) of polyamidoamine or starburst dendrimers (n-SBDs) creating macromol. polychelates. Gadolinium ion was added to the dendrimer polychelates for evaluating the parameters needed to create magnetic resonance imaging (MRI) contrast agents that have long blood circulation times. The resulting water sol. n-SBD-GdDO3As were mono-disperse and ranged from 11 Gd3+ ions per G3 dendrimer (MW 18.4 kDa to 57) Gd3+ ions per G5 dendrimer (MW 61.8 kDa). NMR Dispersion (NMRD) profiles revealed peak relaxivities up to 18.8 mM-1 s-1 at 25 MHz, with the magnitude increasing linearly as a function of mol. wt. Blood elimination half-life in rats increased with mol. wt. ranging from 11(.+-.5) min for 3-SBD-(GdDO3A)24 (22 kDa) to 115(.+-.8) min for the 5-SBD-(GdDO3A)57 (61.8 kDa). Seven-day liver retention increased from 1 to over 40% over the same mol. wt. range. The effects of grafting polyethylene glycol (PEG) onto n-SBD-GdDO3A polychelates were also studied. Relaxivities ranged from 11 to 14.9 mM-1 s-1, blood elimination half-lives increased significantly (range 33-1219 min) and the seven-day liver uptake dropped to 1-8% of the injected dose. However, no correlations between these measurements and mol. wt. were found over the range studied (20.5-69.3 kDa). These results suggest that both the mol. wt. and type of terminal group on the n-SBD-GdDO3A polychelates control the pharmacokinetics and biodistribution of the macromol. contrast agent. The addn. of covalently bound PEG to the n-SBD-GdDO3A surface significantly improved the biol. performance of the contrast agents.

IT **174131-78-3DP**, starburst dendrimers, gadolinium complexes, reaction products with polyethylene glycol derivs.
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Gd(III) DO3A macrocycles and polyethylene glycol coupled to dendrimers: mol. wt. effect on phys. and biol. properties of macromol. MRI contrast agents)

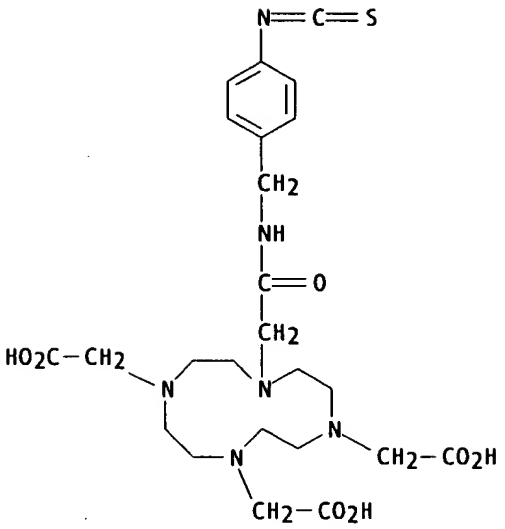
RN 174131-78-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-isothiocyanatophenyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



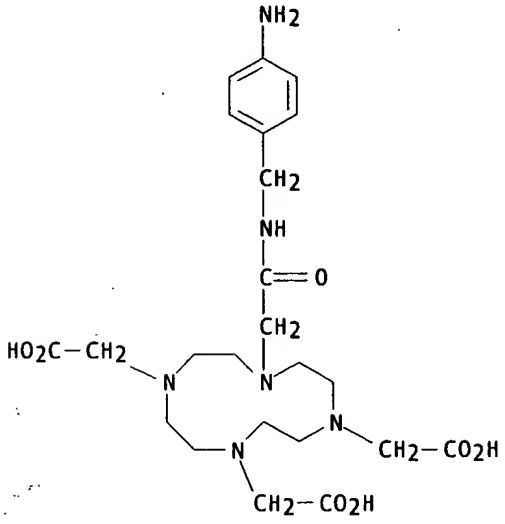
IT **174131-72-7P 174131-78-3P 191403-42-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; Gd(III) DO3A macrocycles and polyethylene glycol coupled to dendrimers: mol. wt. effect on phys. and biol. properties of macromol. MRI contrast agents)
RN 174131-72-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-nitrophenyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 174131-78-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-isothiocyanatophenyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 191403-42-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-aminophenyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



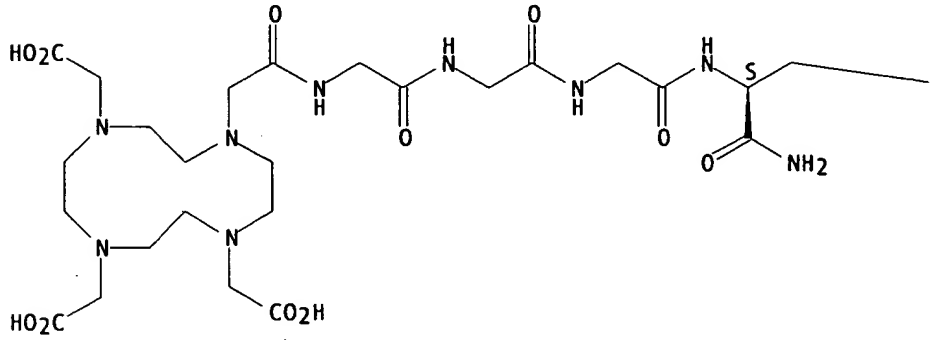
L10 ANSWER 38 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:325414 CAPLUS
DOCUMENT NUMBER: 126:340528
TITLE: A study on pre-labeling method of monoclonal antibody Lym-1 with yttrium-90
AUTHOR(S): Zhong, Gaoren; Zhu, Jianhua; Zhu, Tong
CORPORATE SOURCE: Shanghai Medical University, Shanghai, 200032, Peop. Rep. China
SOURCE: Hejishu (1996), 19(7), 440-444
CODEN: NUTEDL; ISSN: 0253-3219
PUBLISHER: Kexue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A pre-labeling method of monoclonal antibody Lym-1 with 90Y using a new bifunctional chelating agent (DOTA-peptide) was studied. 90Y was first labeled to the bifunctional chelating agent and then conjugated to the monoclonal antibody. The radioactivity yield was 30%. The radiochem. purity of 90Y-labeled Lym-1 was detd. to be over 95% by gel filtration HPLC and silica gel TLC. The immunoreactivity of the final product was found to be greater than 100% relative to 125I-Lym-1 (as a std.) by in vitro cell binding assay.

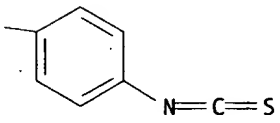
IT 149206-88-2DP, conjugates with monoclonal antibodies and yttrium-90
RL: BAC (Biological activity or effector, except adverse); PNU (Preparation, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(prelabeling method of monoclonal antibody Lym-1 with yttrium-90 using DOTA-peptide as bifunctional chelating agent)
RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



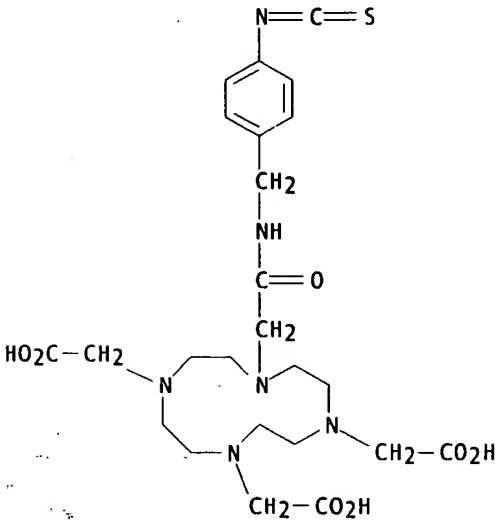
L10 ANSWER 39 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:55427 CAPLUS
DOCUMENT NUMBER: 126:168495
TITLE: High-pressure NMR kinetics. 72. The role of water exchange in attaining maximum relaxivities for dendrimeric MRI contrast agents
AUTHOR(S): Toth, Eva; Pubanz, Dirk; Vauthey, Sylvain; Helm, Lothar; Merbach, Andre E.
CORPORATE SOURCE: Inst. Chimie Minerale et Analytique, Univ. de lausanne, Lausanne, CH-1015, Switz.
SOURCE: Chem.--Eur. J. (1996), 2(12), 1607-1615
Published in: Angew. Chem., Int. Ed. Engl., 35(23/24)
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Macrocyclic GdIII complexes attached to dendrimers represent a new class of potential MRI contrast agents. They have an extended lifetime in the blood pool, which is indispensable for their application in magnetic resonance angiog., and high relaxivities, which reduce the dose required to produce quality images. We performed a variable-temp. and-pressure 170 NMR study in aq. soln. and at 14.1, 9.4, and 1.4 T on the water exchange and rotational dynamics of three macrocyclic GdIII complexes based on polyamidoamine dendrimers, as well as on the GdIII complex of the monomer unit with the linker group. The water exchange rates kex298 for generation 5 [G5(N{CS}N-bz-Gd-{DO3A}{H2O})30], generation 3

[G3(N{CS}N-bz-Gd{DO3A}-{H2O})23], and the monomer [Gd(DO3A-bz-NO2)(H2O)] complexes are 1.5 .+-. 0.1, 1.3 .+-. 0.1, 1.0 .apprxeq. 0.1, and 1.6 .+-. 0.1 .times. 106 s-1, resp., and the activation vols. .DELTA.V.thermod. of water exchange on the latter two compds. are +3.1 .+-. 0.2 and +7.7 .+-. 0.5 cm3 mol-1, indicating dissociatively activated exchange reactions ({CS}N-bz-{DO3A} = 1-(4-isothiocyanatobenzyl)amido-4,7,10-tri(acetic acid)tetrazacyclododecane). The rotational correlation times for the dendrimers are 4 to 8 times longer than for monomeric or dimeric GdIII poly(amino carboxylates). As a consequence of the slow rotation, the proton relaxivities of these dendrimer complexes are considerably higher than those of smaller complexes. However, the low water exchange rates prevent the dendrimer proton relaxivities from attaining the values expected from the increase in the rotational correlation times. Modifications of the chelating ligand may result in a faster water exchange and thus allow the full benefit of slow rotation to be achieved.

IT 174131-78-3D, gadolinium complexes
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of water exchange in attaining max. relaxivities for dendrimeric MRI contrast agents)

RN 174131-78-3 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-isothiocyanatophenyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 40 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:679135 CAPLUS
DOCUMENT NUMBER: 125:315328
TITLE: Polyazacycloalkane compounds
INVENTOR(S): Schultze, Lisa; Bulls, Alan Ray
PATENT ASSIGNEE(S): Nycomed Imaging A.S, Norway
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9628433	A1	19960919	WO 1996-GB464	19960301

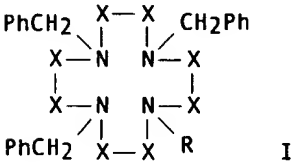
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

US 5631368	A	19970520	US 1995-478755	19950607
US 5677446	A	19971014	US 1995-478754	19950607
CA 2214990	AA	19960919	CA 1996-2214990	19960301
AU 9648391	A1	19961002	AU 1996-48391	19960301
EP 815091	A1	19980107	EP 1996-904204	19960301
R: DE, ES, FR, GB, IT, IE				
CN 1183775	A	19980603	CN 1996-193738	19960301
JP 10511977	T2	19981117	JP 1996-527351	19960301
JP 3059488	B2	20000704		
US 5705637	A	19980106	US 1997-790855	19970203
NO 9704170	A	19971107	NO 1997-4170	19970909
PRIORITY APPLN. INFO.:			GB 1995-4910	19950310
			US 1995-478755	19950607
			WO 1996-GB464	19960301

OTHER SOURCE(S): MARPAT 125:315328

GI



I

AB The prepn. is claimed of tribenzylcyclen compds. (I) (R = H, or a C1-12 alkyl group optionally substituted by hydroxy, alkoxy or aryl groups or R = an amphiphilic aralkyl group comprising a N, S, O or P interrupted C2-25 alkylene chain, e.g. a polyalkylene oxide chain or R provides a bridge to a 2nd tribenzylcyclen group, but with the proviso that R is other than benzyl; X = CHR1, or R = H two X groups = CO groups; and R1 = H, a C1-6alkyl group optionally substituted by hydroxy, alkoxy or carboxy groups or an aralkyl group having 1 to 6 carbons in the alkyl moiety and optionally substituted in the aryl moiety by alkyl, alkoxy, hydroxy or isothiocyanate groups). I are useful in the prepn. of DO3A, N-substituted-1,4,7,10-tetraazacyclododecane-N',N'',N'''-triacetic acids, and the phosphonic acid analogs and their Gd complexes.

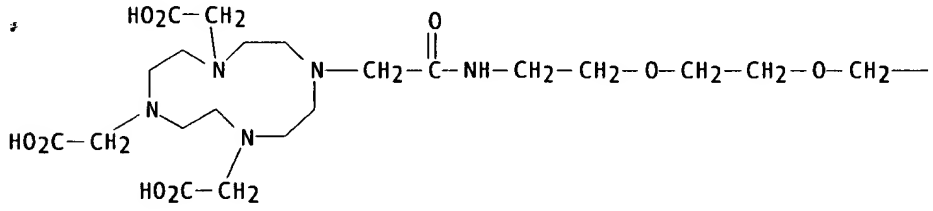
IT **167407-72-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of gadolinium polyalkylene complexes)

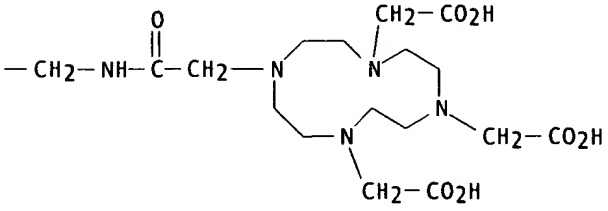
RN 167407-72-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(2,13-dioxo-6,9-dioxa-3,12-diazatetradecane-1,14-diyl)bis- (9CI) (CA INDEX NAME)

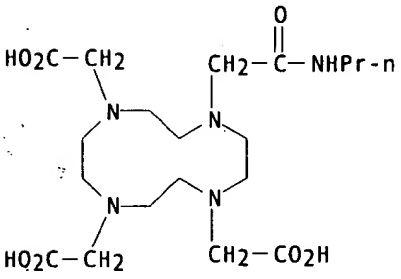
PAGE 1-A



PAGE 1-B



L10 ANSWER 41 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:653416 CAPLUS
DOCUMENT NUMBER: 126:80220
TITLE: Molecular Mechanics Investigation of Gadolinium(III) Complexes
AUTHOR(S): Reichert, David E.; Hancock, Robert D.; Welch, Michael J.
CORPORATE SOURCE: Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Inorg. Chem. (1996), 35(24), 7013-7020
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Parameters for the com. available modeling package SYBYL have been developed for Gd3+ complexes allowing these to be studied with mol. mechanics. With these parameters and a technique termed the "coordination scan", the coordination nos. of Gd(III) based complexes can be predicted, and thus the hydration no. q detd. Knowledge of q has allowed the prediction of molar relaxivities based on correlations to literature values. In addn., the calcd. value .DELTA.Ecoord was found to successfully predict the thermodn. stability consts. for polyamino carboxylate ligands with Gd3+. Gadolinium complexes are commonly utilized as MRI contrast agents, and thus the techniques utilized in this work should aid in the development of new contrast agents.
IT 118476-80-5
RL: PRP (Properties)
(mol. mechanics parameters and techniques for gadolinium(III) complexes)
RN 118476-80-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-(propylamino)ethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 42 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:425321 CAPLUS
DOCUMENT NUMBER: 125:80777
TITLE: Chelate-containing liposomal agents, and their preparation, for diagnostic imaging and therapeutic use
INVENTOR(S): Garrity, Martha; Varadarajan, John; Watson, Alan David
PATENT ASSIGNEE(S): Cockbain, Julian Roderick Michaelson, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611023	A1	19960418	WO 1995-GB2378	19951009

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2200867	AA	19960418	CA 1995-2200867	19951009
AU 9536136	A1	19960502	AU 1995-36136	19951009
EP 785804	A1	19970730	EP 1995-933505	19951009
R: DE, ES, FR, GB, IE, IT				
CN 1168636	A	19971224	CN 1995-196533	19951009
JP 10507172	T2	19980714	JP 1995-512427	19951009
US 6045821	A	20000404	US 1997-809729	19970529
PRIORITY APPLN. INFO.:			GB 1994-20390	19941010
			WO 1995-GB2378	19951009

OTHER SOURCE(S): MARPAT 125:80777

AB A liposomal agent is provided which comprises liposomes having bound to a membrane thereof a chelated diagnostically or therapeutically effective metal ion, the chelating agent binding the metal ion having a macrocyclic chelant moiety with, attached to a single ring atom thereof, a lipophilic membrane assocg. moiety. The liposomes of the invention are useful for e.g. diagnostic imaging agents.

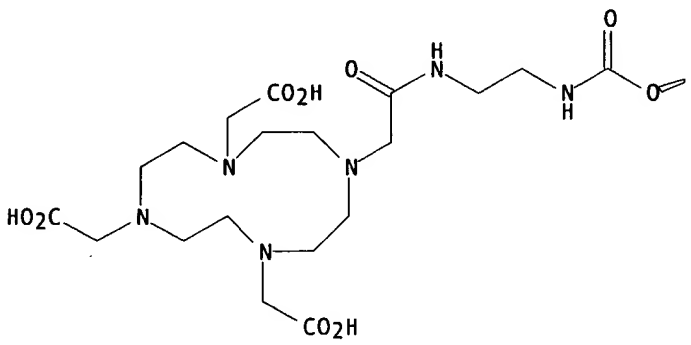
IT **173308-28-6**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chelate-contg. liposomal agents, and their prepn., for diagnostic imaging and therapeutic use)

RN 173308-28-6 CAPLUS

CN Cholest-5-en-3-ol (3.beta.)-, [2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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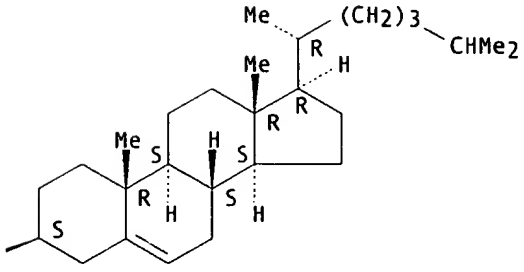
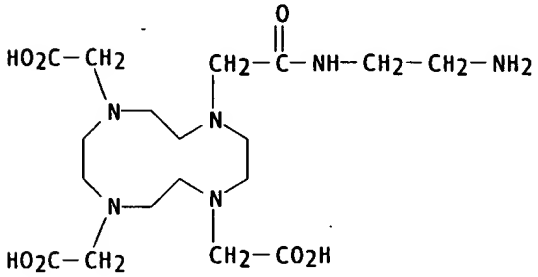
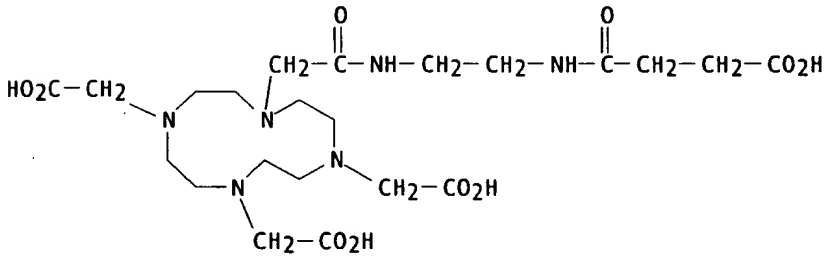


IT 150467-20-2P 173308-24-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction; chelate-contg. liposomal agents, and their prepn., for diagnostic imaging and therapeutic use)
RN 150467-20-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 173308-24-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[(3-carboxy-1-oxopropyl)amino]ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 43 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:367296 CAPLUS
DOCUMENT NUMBER: 125:58999
TITLE: Preparation of conjugates of metal complexes with modified oligonucleotides for use in diagnosis and/or therapy.
INVENTOR(S): Dinkelborg, Ludger; Hilger, Christoph-Stephan; Niedballa, Ulrich; Platzek, Johannes; Raduechel, Bernd; Speck, Ulrich; Gold, Larry; Pieken, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Germany; Nexstar Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

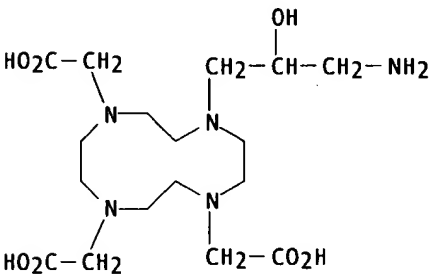
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602274	A1	19960201	WO 1995-EP2539	19950630
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 4424922	A1	19960118	DE 1994-4424922	19940714
DE 4445078	A1	19960613	DE 1994-4445078	19941205
AU 9529791	A1	19960216	AU 1995-29791	19950630
EP 777498	A1	19970611	EP 1995-925792	19950630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10503182	T2	19980324	JP 1995-504630	19950630

NO 9700141 A 19970314 NO 1997-141 19970113
PRIORITY APPLN. INFO.: DE 1994-4424922 19940714
DE 1994-4445078 19941205
WO 1995-EP2539 19950630

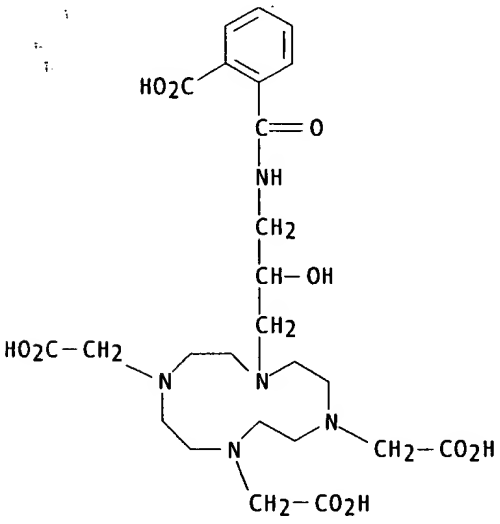
AB Oligonucleotide conjugates contg. a modified oligonucleotide radical stabilized to degrdn. by nucleases and substituents BK where B = bond, connecting component, K = complexing agent or complex of radioactive metal isotopes or stable isotopes which can be converted by outside radiation to radioactive isotopes, or which convert radiation from outside to radiation of different quality, energy content, and/or different wavelength, of elements of at. nos. 5, 21-29, 31, 42-44, 49, 57-83, or 85, were prepd. for radiodiagnosis and/or radiotherapy (no data). Thus, the 5'-(6-amino-1-hexylphosphonic acid ester) of 5'-CUCAUGGAGCGCAAGACGAAUAGCUACAUAT*T*T*T*T-3' (* = methylphosphonate bond) (prepn. given) was stirred with 2-(4-isothiocyanatobenzyl)diethylenetriamine-N,N'N',N'',N''-pentaacetic acid in NaHCO3/Na2CO3 buffer at room temp. to give the corresponding thiourea conjugate. Prepn. of the yttrium-90 complex of the latter is described.

IT **146270-94-2P 174700-60-8P 174700-61-9P**
174700-62-0P 174700-63-1P 177747-34-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of conjugates of metal complexes with modified oligonucleotides for use in diagnosis and/or therapy)

RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)

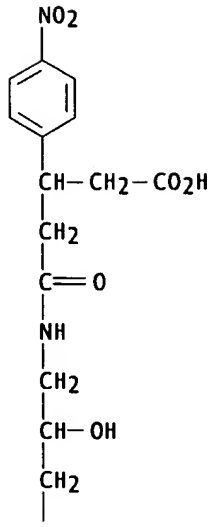


RN 174700-60-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(2-carboxybenzoyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

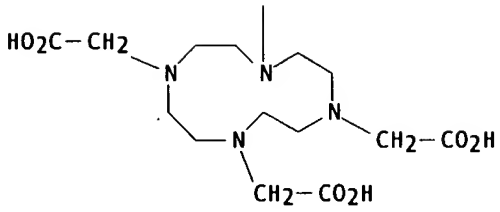


RN 174700-61-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-nitrophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

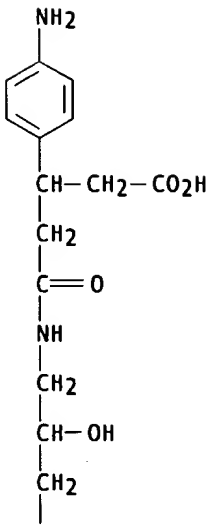


PAGE 2-A



RN 174700-62-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[3-(4-aminophenyl)-4-carboxy-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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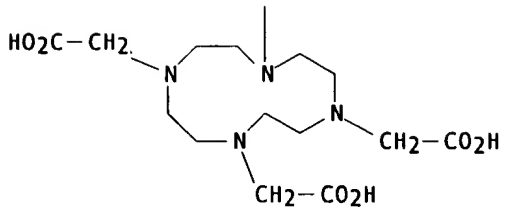
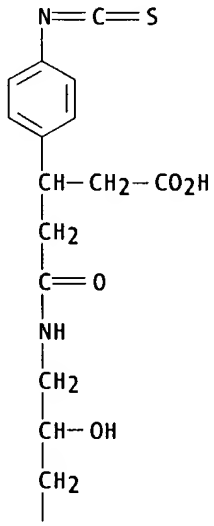
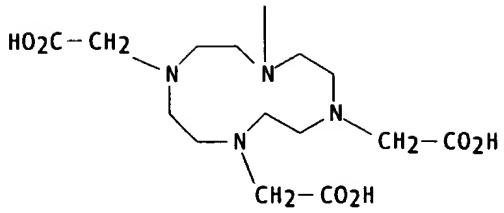


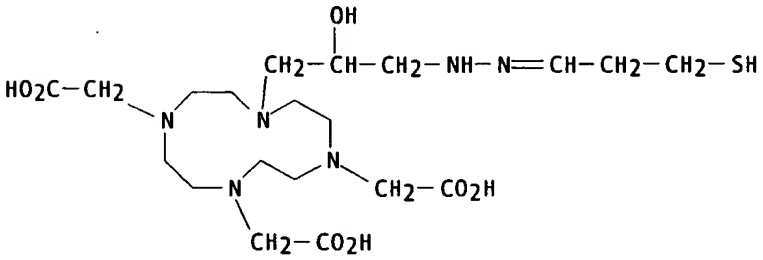
RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



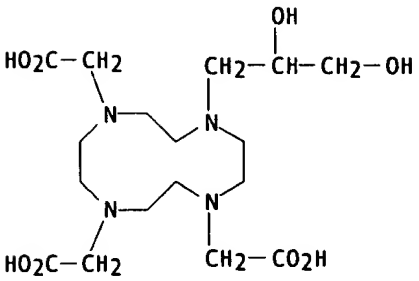


RN 177747-34-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(3-mercaptopropylidene)hydrazino]propyl]- (9CI) (CA INDEX NAME)

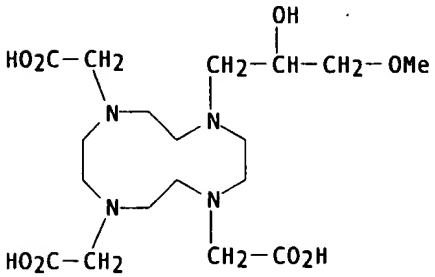


L10 ANSWER 44 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:358485 CAPLUS
DOCUMENT NUMBER: 125:68991
TITLE: Selectivity of macrocyclic aminocarboxylates for alkaline-earth metal ions and stability of their complexes
AUTHOR(S): Chang, C. Allen
CORPORATE SOURCE: Inst. Biol. Sci. Technol., Natl. Chiao Tung Univ., Hsinchu, 30039, Taiwan
SOURCE: J. Chem. Soc., Dalton Trans. (1996), (11), 2347-2350
CODEN: JCDTBI; ISSN: 0300-9246
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The stability consts. of alk.-earth-metal complexes of several macrocycles derived from 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (H3L1) were detd. by the potentiometric pH-titrn. method. The derivs. are formed by variation of the substituent R at N10, i.e. R = Prn (H3L2), CH2C6H4NO2-p (H3L3), CH2CH(OH)CH3 (H3L4), CH2CH(OH)CH2OH (H3L5), CH2CH(OH)CH2OCH3 (H3L6) and CH2CO2H (H4L7). In general, the stabilities of these complexes are greater than those with non-cyclic ligands except in a few cases, e.g. trans-1-cyclohexane-1,2-diyldinitrilotetraacetic acid (H4cdta). For H3L1-H3L3, the stability trend is CaL > MgL > SrL > BaL; for H3L4-H3L6 and H4L7, CaL > SrL > BaL > MgL. The former trend is similar to those found for smaller, non-cyclic ligands with six or less donor atoms such as H4cdta. The latter trend is the same as that for the larger, more flexible, and calcium-selective ligand ethylenedioxydiethylenedinitrilotetraacetic acid. The selectivity of H3L4-H3L6 and H4L7 for Ca2+, Sr2+ and Ba2+ over Mg2+ ion is presumably due to their ability to sat. the octahedral co-ordination environment of Mg2+ while still allowing the larger Ca2+, Sr2+ and Ba2+ to be fully eight-coordinated.
IT 114873-42-6 136687-96-2
RL: PRP (Properties); RCT (Reactant)
(protonation consts. of macrocyclic aminocarboxylates and their selectivity for alk.-earth metal ions)
RN 114873-42-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3-

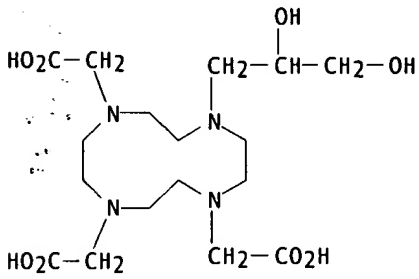
dihydroxypropyl)- (9CI) (CA INDEX NAME)



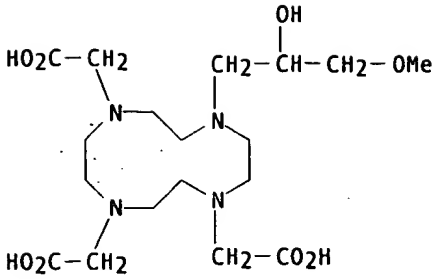
RN 136687-96-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-3-methoxypropyl)- (9CI) (CA INDEX NAME)



IT 114873-42-6D, alk.-earth-metal complexes 136687-96-2D, alk.-earth-metal complexes
RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)
(selectivity of macrocyclic aminocarboxylates for alk.-earth metal ions and stability of their complexes)
RN 114873-42-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3-dihydroxypropyl)- (9CI) (CA INDEX NAME)



RN 136687-96-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-3-methoxypropyl)- (9CI) (CA INDEX NAME)



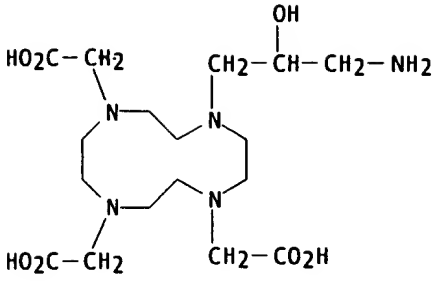
L10 ANSWER 45 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:332412 CAPLUS
DOCUMENT NUMBER: 125:5077
TITLE: Conjugates of metal complexes and oligonucleotides, which specifically bond to specific target structures and their uses in NMR diagnosis.
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduechel, Bernd; Muehler, Andreas; Speck, Ulrich; Berndorff, Dietmar; Gold, Larry; Pieken, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Germany; Nexstar Pharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602669	A1	19960201	WO 1995-EP2686	19950712
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 4424923	A1	19960118	DE 1994-4424923	19940714
DE 4445076	A1	19960613	DE 1994-4445076	19941205
AU 9531090	A1	19960216	AU 1995-31090	19950712
EP 770146	A1	19970502	EP 1995-926850	19950712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10511842	T2	19981117	JP 1995-504000	19950712
PRIORITY APPLN. INFO.:			DE 1994-4424923	19940714
			DE 1994-4445076	19941205
			WO 1995-EP2686	19950712

AB This invention relates to chem. modified oligonucleotide conjugates that contain a complexing agent or a complex that is bound by a connecting component to the oligonucleotides. In this case, the oligonucleotides are modified in a way that prevents or at least significantly inhibits the degrdn. by naturally occurring nucleases. The oligonucleotide radical can bond specifically and with high bonding affinity to target structures and can thus produce a specific therapeutic or diagnostic effect by the bound complexing agent or complex. 5'-(6-Amino-1-hexylphosphoric acid ester) of a 32mer-oligonucleotide was modified and coupled with 111In(III) acetate. This conjugate can be use for NMR diagnosis.

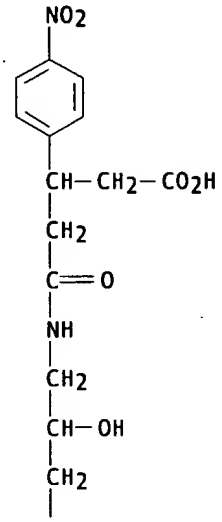
IT 146270-94-2P 174700-61-9P 174700-62-0P
174700-63-1DP, conjugates with 32mer oligonucleotide, indium-111 complex 174700-63-1P 177179-42-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of metal complex-oligonucleotide conjugates uses in NMR diagnosis)

RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)

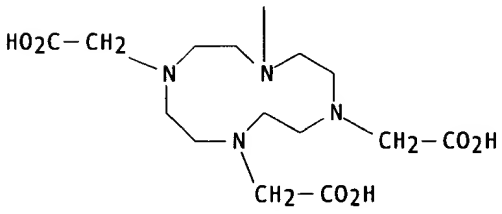


RN 174700-61-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-nitrophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

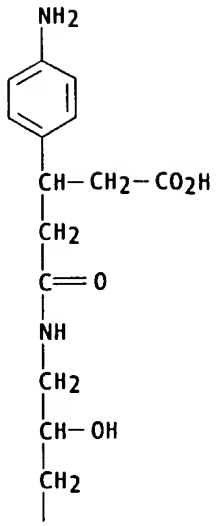


PAGE 2-A



RN 174700-62-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[3-(4-aminophenyl)-4-carboxy-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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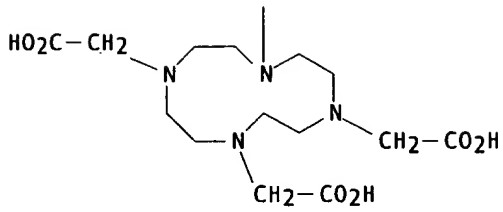
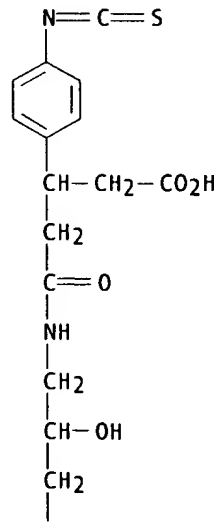


RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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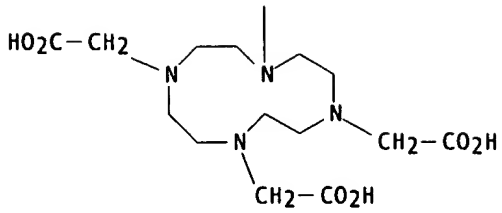
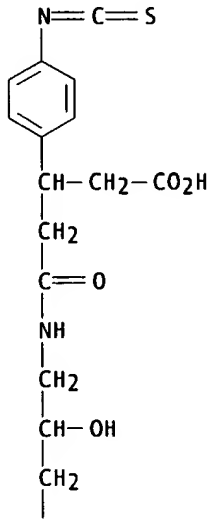


RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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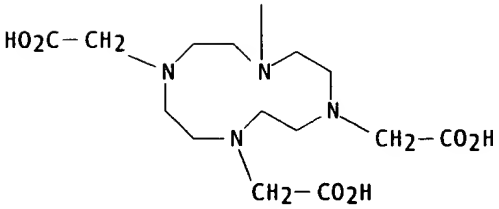
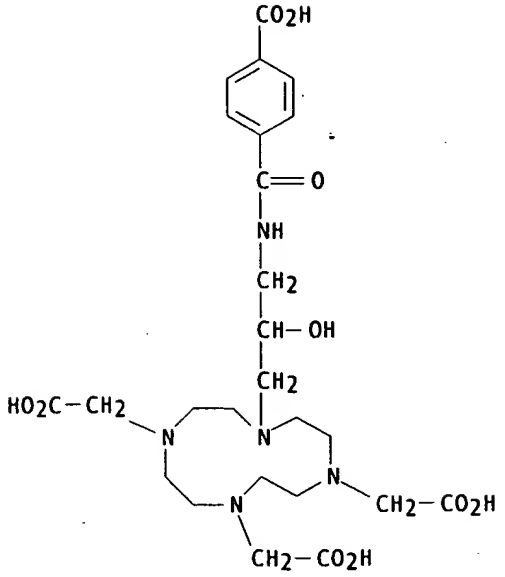
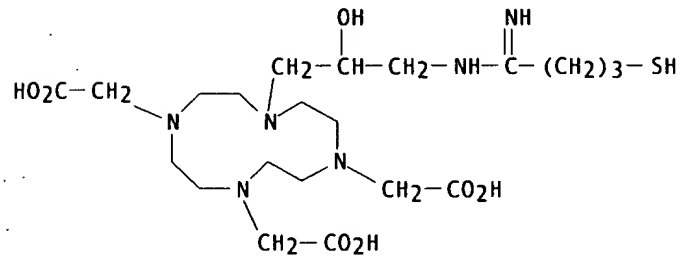


RN 177179-42-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(4-carboxybenzoyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

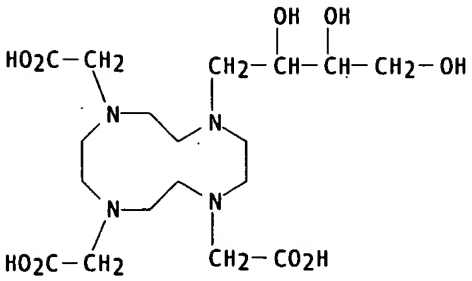


IT 174701-09-8DP, conjugates with 33-mer oligonucleotide, gadolinium complex
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of metal complex-oligonucleotide conjugates uses in NMR diagnosis)
RN 174701-09-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(1-imino-4-mercaptobutyl)amino]propyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 46 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:196247 CAPLUS
DOCUMENT NUMBER: 124:343242
TITLE: One-Stage Monosubstitution in Cyclen - Two Novel Examples
AUTHOR(S): Formanovsky, A. A.; Mikhura, I. V.
CORPORATE SOURCE: Institute of Bioorganic Chemistry, Moscow, 117871, Russia
SOURCE: Synth. Commun. (1996), 26(8), 1595-603
CODEN: SYNCAV; ISSN: 0039-7911
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two new routes for alkyl substitution of one in 4 amino groups in 1,4,7,10-tetraazacyclododecane (cyclen) was described. Isomeric N-tris(hydroxy)butylcyclens were thus obtained in very good yields. Further carboxymethylation of other three amino groups afforded 10-tris(hydroxy)butyl-1,4,7-tris(carboxymethyl)cyclen.
IT 138147-53-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(selective monosubstitution and alkylation of cyclen)
RN 138147-53-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3,4-

trihydroxybutyl)- (9CI) (CA INDEX NAME)



L10 ANSWER 47 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:184037 CAPLUS
DOCUMENT NUMBER: 124:254781
TITLE: Conjugates of metal complexes and oligoribonucleotides which bind specifically to selected target structures
INVENTOR(S): Dinkelborg, Ludger; Hilger, Christoph-Stephan; Niedballa, Ulrich; Platzek, Johannes; Raduechel, Bernd; Speck, Ulrich
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 25 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4424922	A1	19960118	DE 1994-4424922	19940714
CA 2194558	AA	19960201	CA 1995-2194558	19950630
WO 9602274	A1	19960201	WO 1995-EP2539	19950630
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9529791	A1	19960216	AU 1995-29791	19950630
EP 777498	A1	19970611	EP 1995-925792	19950630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1152879	A	19970625	CN 1995-194000	19950630
HU 76329	A2	19970828	HU 1997-100	19950630
JP 10503182	T2	19980324	JP 1995-504630	19950630
ZA 9505895	A	19960219	ZA 1995-5895	19950714
NO 9700141	A	19970314	NO 1997-141	19970113
AU 9920360	A1	19990617	AU 1999-20360	19990312
AU 721330	B2	20000629		

PRIORITY APPLN. INFO.:
DE 1994-4424922 19940714
DE 1994-4445078 19941205
AU 1995-29791 19950630
WO 1995-EP2539 19950630

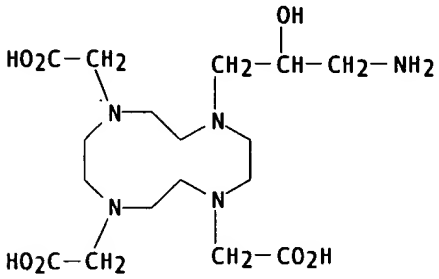
AB Conjugates of modified oligonucleotides with complexes of radioactive or stable metal isotopes, which bind specifically to biol. target structures, are useful in diagnostic imaging and radiotherapy. The oligonucleotides are modified to render them resistant to degrdn. by endogenous nucleases, e.g. by O-alkylation, halogenation, amination, or redn. at the 2' position or by replacement of phosphodiester groups by phosphorothioate, phosphorodithioate, or alkylphosphonate linkages. The oligonucleotides are selected from a random mixt. for binding to a target such as a non-nucleic acid macromol., tissue, or organ. Thus, a 30-mer oligonucleotide ligand for NGF was conjugated with the linker .beta.-cyanoethyl N,N-diisopropylamino-6-(trifluoroacetamido)-1-hexylphosphoramidite, then with 10-[7-(4-isothiocyanatophenyl)-2-hydroxy-5-oxo-7-(carboxymethyl)-4-azaheptyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane (prepn. given), and complexed with 111In(III) for

use as a radiodiagnostic agent.

IT **146270-94-2P 174700-60-8P 174700-61-9P**
174700-62-0P 174700-63-1P 174701-09-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(conjugates of metal complexes and oligoribonucleotides which bind specifically to selected target structures)

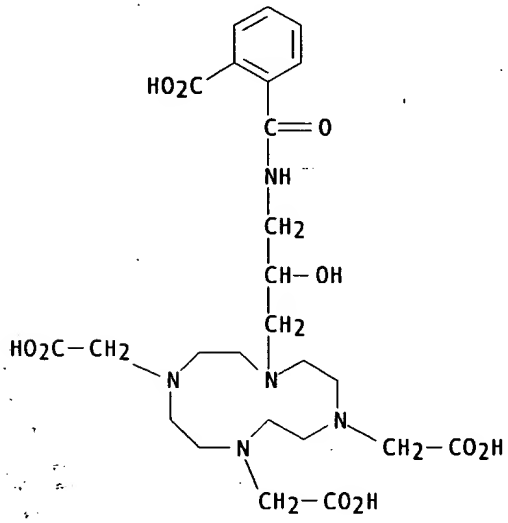
RN 146270-94-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



RN 174700-60-8 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(2-carboxybenzoyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 174700-61-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-nitrophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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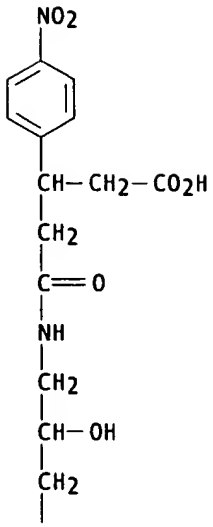

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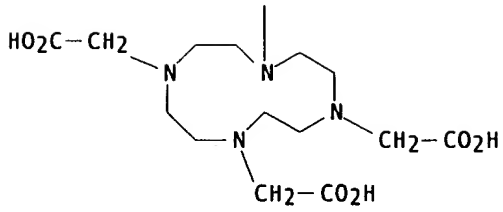

RN 174700-62-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[3-(4-aminophenyl)-4-carboxy-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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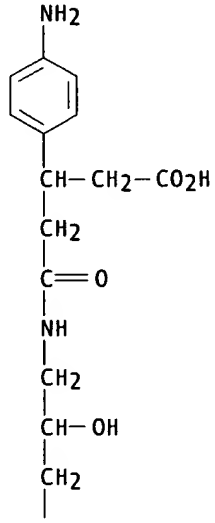

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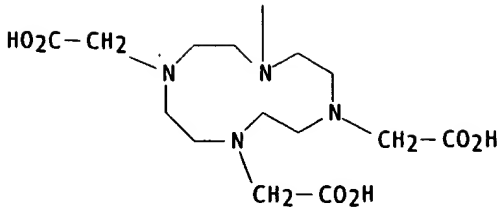
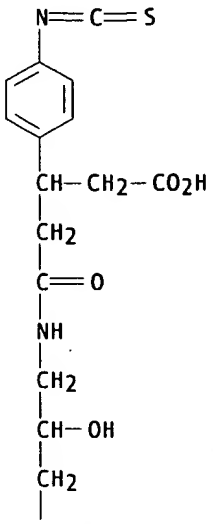


RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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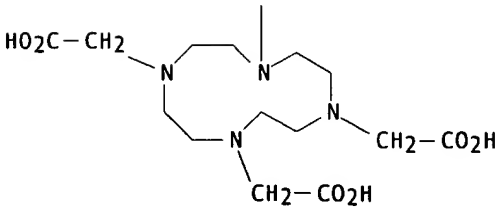
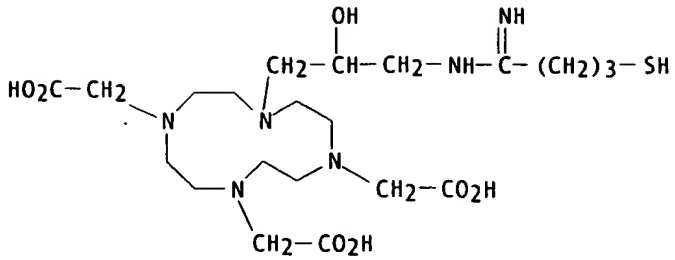


RN 174701-09-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(1-imino-4-mercaptobutyl)amino]propyl]- (9CI) (CA INDEX NAME)



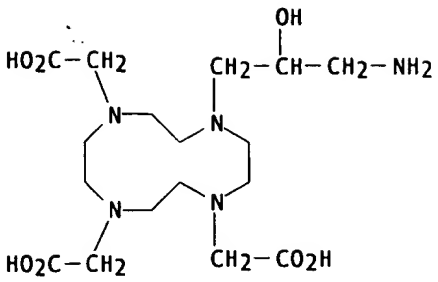
L10 ANSWER 48 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:184036 CAPLUS
DOCUMENT NUMBER: 124:283703
TITLE: Conjugates of metal complexes and oligoribonucleotides which bind specifically to selected target structures for MRI
INVENTOR(S): Platzek, Johannes; Niedballa, Ulrich; Raduechel, Bernd; Muehler, Andreas; Speck, Ulrich
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4424923	A1	19960118	DE 1994-4424923	19940714
WO 9602669	A1	19960201	WO 1995-EP2686	19950712
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9531090	A1	19960216	AU 1995-31090	19950712
EP 770146	A1	19970502	EP 1995-926850	19950712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10511842	T2	19981117	JP 1995-504000	19950712
ZA 9505894	A	19960730	ZA 1995-5894	19950714
PRIORITY APPLN. INFO.:			DE 1994-4424923	19940714
			DE 1994-4445076	19941205
			WO 1995-EP2686	19950712

AB Conjugates of modified oligonucleotides with metal complexes or complexing agents, which bind specifically to biol. target structures, are useful in diagnostic NMR imaging. The oligonucleotides are modified to render them resistant to degrdn. by endogenous nucleases, e.g. by O-alkylation, halogenation, amination, or redn. at the 2' position or by replacement of phosphodiester groups by phosphorothioate, phosphorodithioate, or alkylphosphonate linkages. The oligonucleotides are selected from a random mixt. for binding to a target such as a non-nucleic acid macromol., tissue, or organ. Thus, a 30-mer oligonucleotide ligand for serine proteinase was conjugated with the linker .beta.-cyanoethyl S-trityl-6-mercaptohexyl N,N-diisopropylphosphoramidite, then with 1,4,7,10-tetraaza-2-[(5-aza-8-maleimido-6-oxo)octyl]cyclododecane-1,4,7,10-tetraacetic acid, and complexed with Gd3+ for use in NMR imaging.

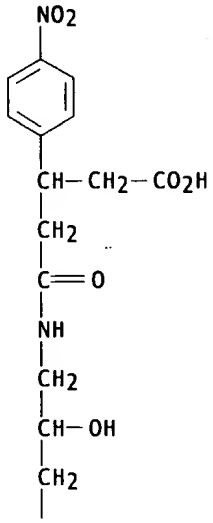
IT 146270-94-2DP, gadolinium complexes 174700-61-9DP, gadolinium complexes 174700-62-0DP, gadolinium complexes 174700-63-1DP, gadolinium complexes
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates of metal complexes and oligoribonucleotides which bind specifically to selected target structures for MRI)

RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



RN 174700-61-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-nitrophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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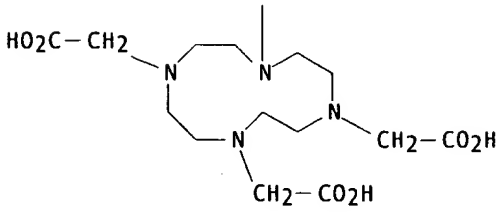
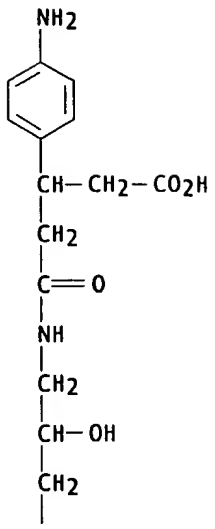


RN 174700-62-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[3-(4-aminophenyl)-4-carboxy-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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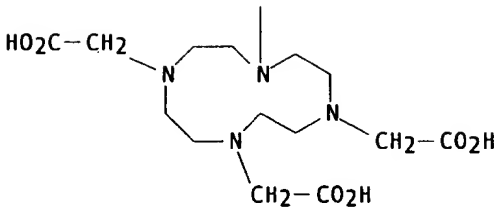
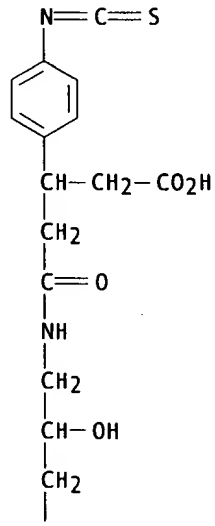
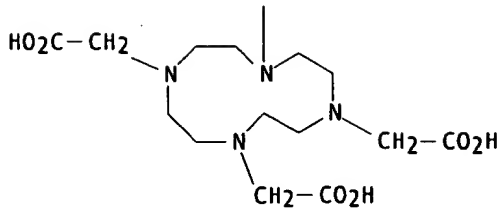


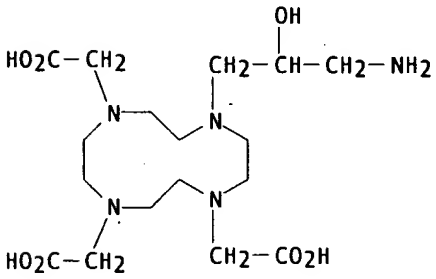
RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

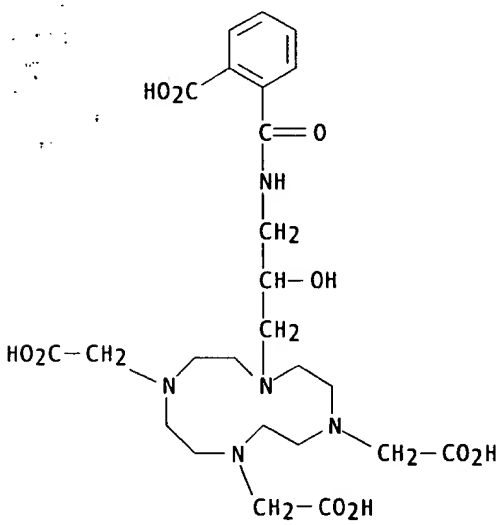




IT 146270-94-2P 174700-60-8P 174700-61-9P
174700-62-0P 174700-63-1P 174701-09-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(conjugates of metal complexes and oligoribonucleotides which bind specifically to selected target structures for MRI)
RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)

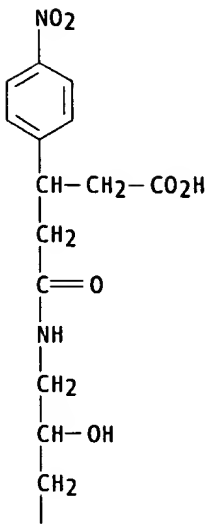


RN 174700-60-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(2-carboxybenzoyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 174700-61-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-nitrophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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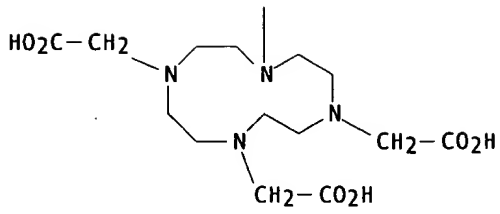

RN 174700-62-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[3-(4-aminophenyl)-4-carboxy-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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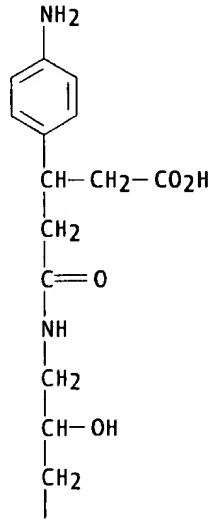

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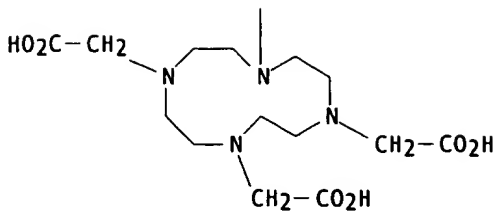

RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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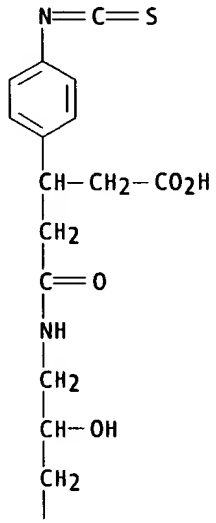

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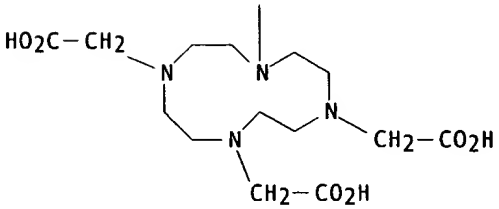
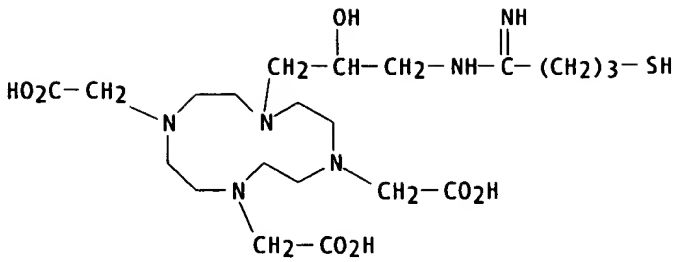


RN 174701-09-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(1-imino-4-mercaptobutyl)amino]propyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 49 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:184035 CAPLUS
DOCUMENT NUMBER: 124:232789
TITLE: Preparation of gadolinium-polyamine complexes for radiopharmaceuticals
INVENTOR(S): Schmitt-Willich, Heribert; Platzek, Johannes; Niedballa, Ulrich; Raduechel, Bernd; Muehler, Andreas; Frenzel, Thomas; Ebert, Wolfgang
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 53 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

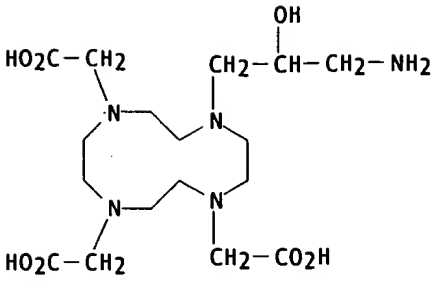
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4425857	A1	19960111	DE 1994-4425857	19940707
WO 9601655	A1	19960125	WO 1995-EP2577	19950704
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2194560	AA	19960125	CA 1995-2194560	19950704
AU 9529808	A1	19960209	AU 1995-29808	19950704
AU 697203	B2	19981001		
EP 768898	A1	19970423	EP 1995-925817	19950704
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1151701	A	19970611	CN 1995-193803	19950704
HU 76804	A2	19971128	HU 1997-25	19950704
JP 10502679	T2	19980310	JP 1995-504100	19950704
ZA 9505682	A	19960222	ZA 1995-5682	19950707
NO 9700055	A	19970306	NO 1997-55	19970107
PRIORITY APPLN. INFO.:			DE 1994-4425857	19940707
			WO 1995-EP2577	19950704

OTHER SOURCE(S): MARPAT 124:232789

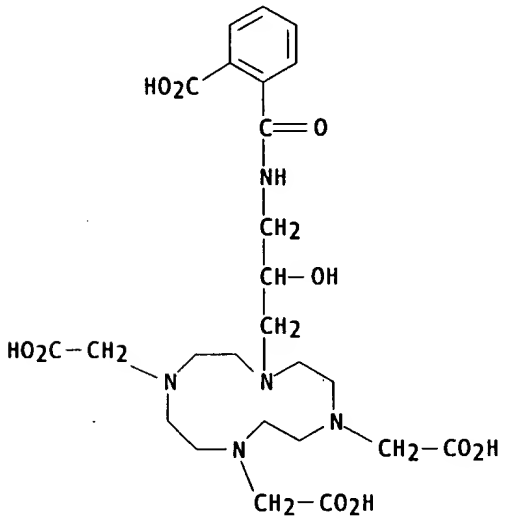
AB Gd-amine complexes are prepd. for use as radiopharmaceuticals. Thus, a Gd-DTPA monoamide complex based on N,N,N',N',N'',N''-hexakis[(2-trilysylamino)ethyl]trimesic acid amide was prepd. from Gd3O3, DTPA and the corresponding amine.

IT **146270-94-2P 174700-60-8P 174700-94-8P 174700-95-9P 174701-00-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of gadolinium-amine complexes for radiopharmaceuticals)

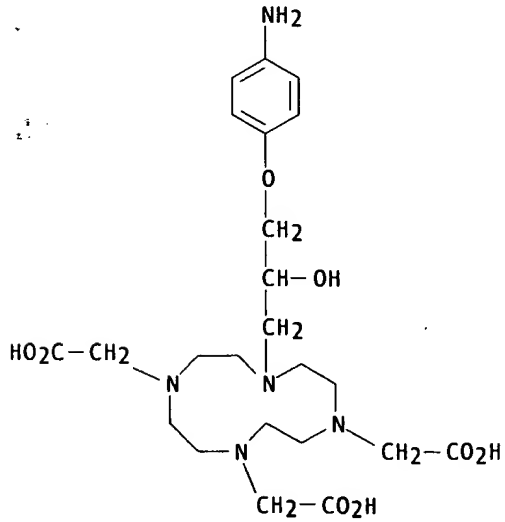
RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



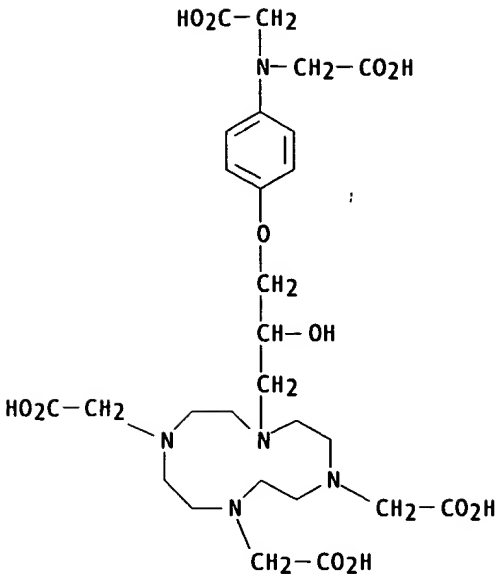
RN 174700-60-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(2-carboxybenzoyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



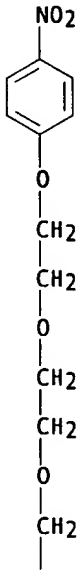
RN 174700-94-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-(4-aminophenoxy)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

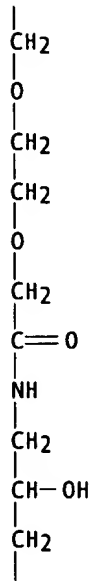


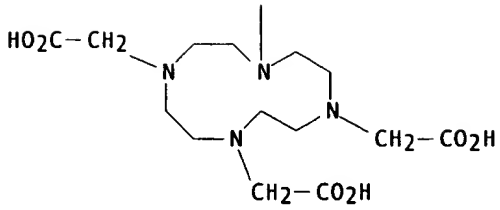
RN 174700-95-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-[bis(carboxymethyl)amino]phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 174701-00-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-18-(4-nitrophenoxy)-5-oxo-7,10,13,16-tetraoxa-4-azaoctadec-1-yl]- (9CI) (CA INDEX NAME)







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RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of gadolinium-amine complexes for radiopharmaceuticals)

RN 146270-94-2 CAPLUS

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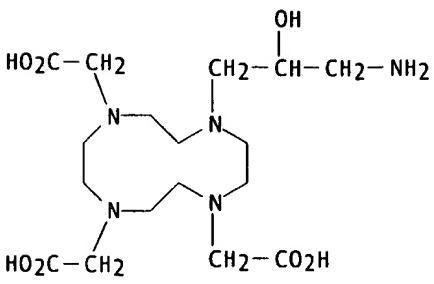

RN 174700-61-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-nitrophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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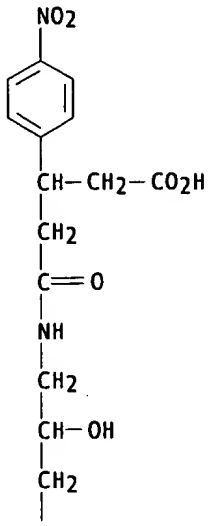

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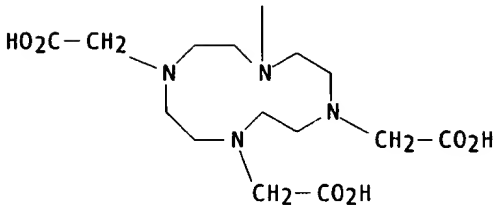
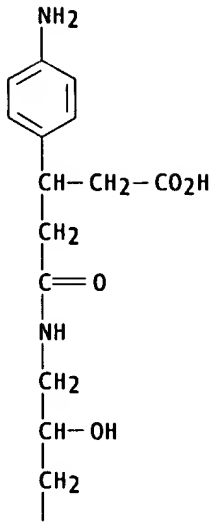


RN 174700-62-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[3-(4-aminophenyl)-4-carboxy-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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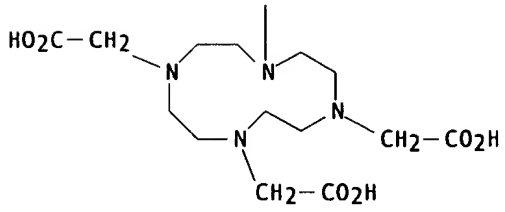

RN 174700-63-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[4-carboxy-3-(4-isothiocyanatophenyl)-1-oxobutyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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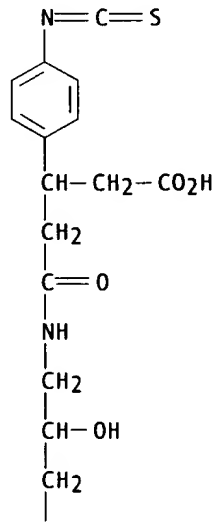

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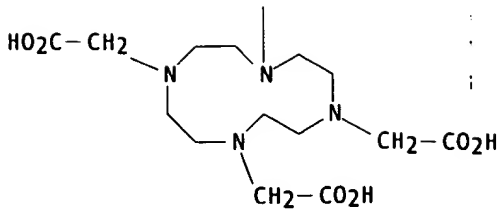

RN 174700-64-2 CAPLUS
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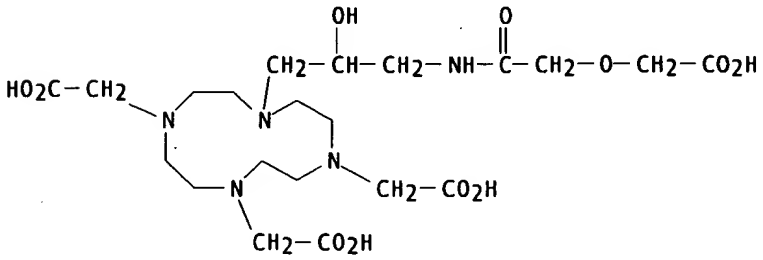

RN 174700-89-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[(4-amino-2-carboxyphenoxy)acetyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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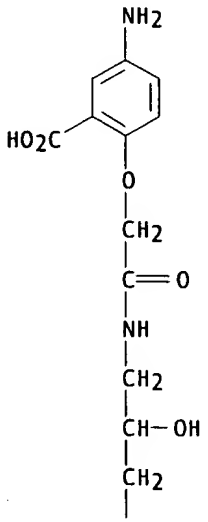

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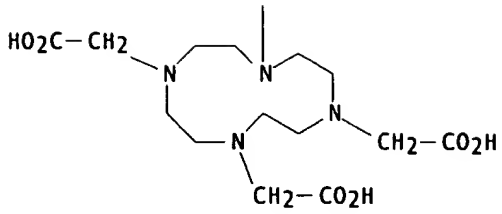
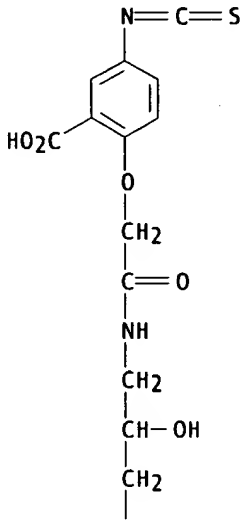
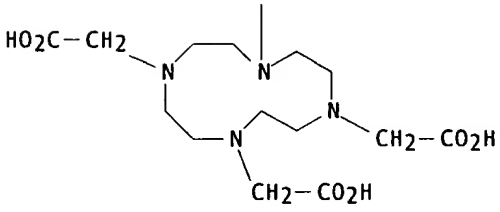


RN 174700-90-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[(2-carboxy-4-isothiocyanatophenoxy)acetyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

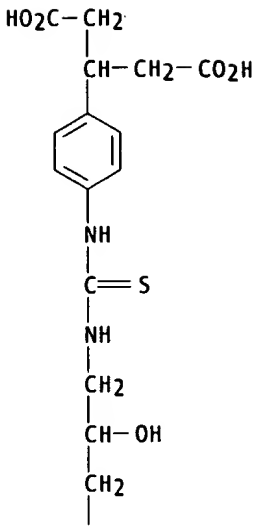
PAGE 1-A

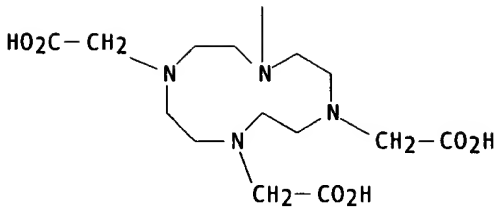


PAGE 2-A

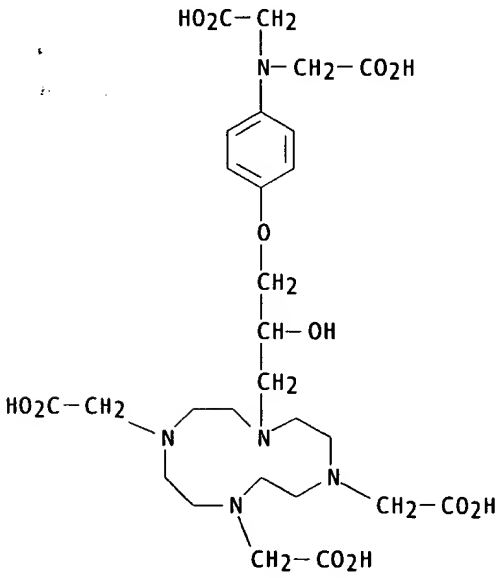


RN 174700-92-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[[[4-[2-carboxy-1-(carboxymethyl)ethyl]phenyl]amino]thioxomethyl]amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)





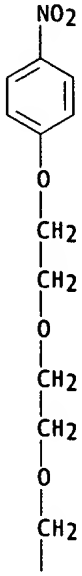
RN 174700-95-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-[bis(carboxymethyl)amino]phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



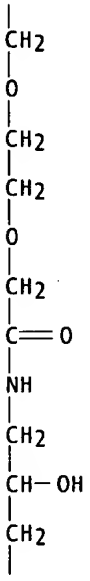
RN 174701-00-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-18-(4-nitrophenoxy)-5-oxo-7,10,13,16-tetraoxa-4-azaoctadec-1-yl]- (9CI) (CA INDEX NAME)

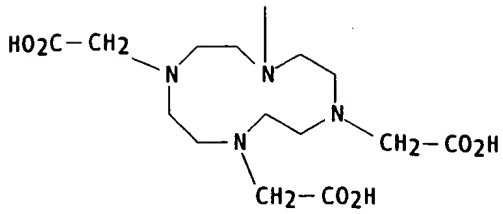
PAGE 1-A



PAGE 2-A

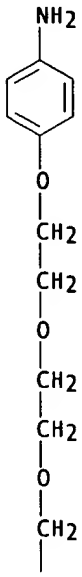


PAGE 3-A

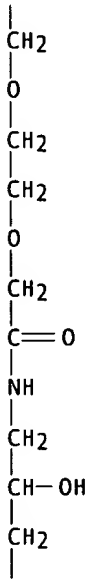


RN 174701-01-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[18-(4-aminophenoxy)-2-hydroxy-5-oxo-7,10,13,16-tetraoxa-4-azaoctadec-1-yl]-(9CI) (CA INDEX NAME)

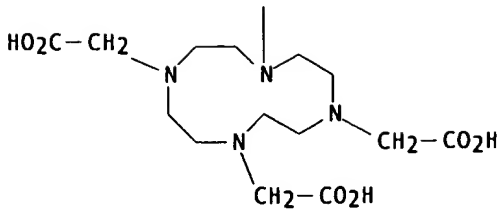
PAGE 1-A



PAGE 2-A

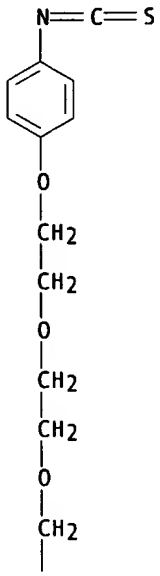


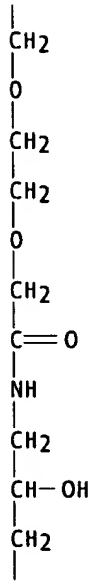
PAGE 3-A

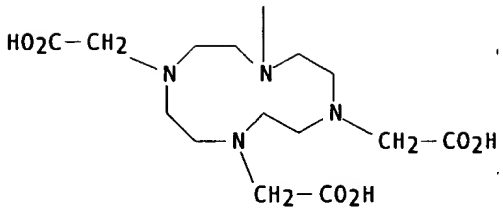


RN 174701-02-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-18-(4-isothiocyanatophenoxy)-5-oxo-7,10,13,16-tetraoxa-4-azaoctadec-1-yl]- (9CI) (CA INDEX NAME)

PAGE 1-A







L10 ANSWER 50 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:155211 CAPLUS
DOCUMENT NUMBER: 124:305463
TITLE: A new approach to hepatospecific MRI contrast agents: gadolinium complexes conjugated to iodinated synthons
AUTHOR(S): Anelli, Pier Lucio; Calabi, Luisella; de Haen, Christoph; Fedeli, Franco; Losi, Pietro; Murru, Marcella; Uggeri, Fulvio
CORPORATE SOURCE: Centro Ricerche Milano, Bracco S.p.A., Milan, I-20134, Italy
SOURCE: Gazz. Chim. Ital. (1996), 126(2), 89-97
CODEN: GCITA9; ISSN: 0016-5603
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The use of biliary iodinated x-ray contrast agents as an address moiety to transport Gd complexes into hepatocytes was studied. Conjugates contg. a Gd chelating subunit (tetraazacyclododecanetetraacetic acid and diethylenetetraaminepentaacetic acid) and an iodinated subunit were designed and synthesized. This series takes into account structural features such as: nature of the iodinated address moiety, overall charge of the conjugate and distance between the two subunits. Preliminary physicochem. and pharmacol. screenings show, for conjugates in which the Gd complex is linked through a spacer to a unit of iopanoic acid: (i) r1 values of >18 (mM s)-1 in human serum, reflecting a strong interaction with human serum albumin; (ii) biliary elimination in rats >65%. Iopanoic acid can be used successfully as an address for the prepn. of conjugates which are promising candidates as hepatospecific MRI contrast agents.

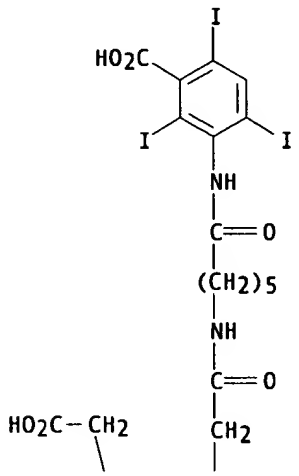
IT **160982-32-1P 160982-33-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(for prepn. of gadolinium MRI contrast agents)

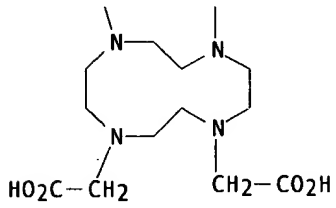
RN 160982-32-1 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[(3-carboxy-2,4,6-triiodophenyl)amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

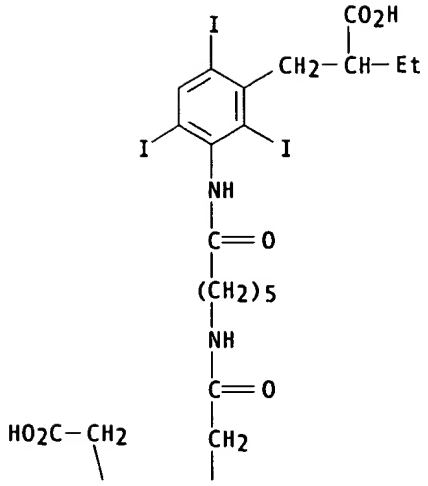


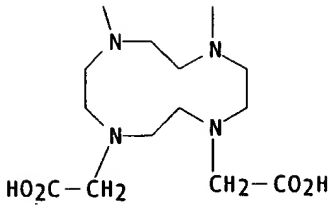
PAGE 2-A



RN 160982-33-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[3-(2-carboxybutyl)-2,4,6-triiodophenyl]amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)





L10 ANSWER 51 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:150262 CAPLUS
DOCUMENT NUMBER: 124:192411
TITLE: Bile acid conjugates, derivatives thereof with metal complexes and related uses
INVENTOR(S): Anelli, Pier Lucio; De Haen, Christoph; Lattuada, Luciano; Morosini, Pierfrancesco; Uggeri, Fulvio
PATENT ASSIGNEE(S): Bracco S.P.A., Italy; Dibra S.P.A.
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532741	A1	19951207	WO 1995-EP1958	19950523
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9525664	A1	19951221	AU 1995-25664	19950523
EP 760683	A1	19970312	EP 1995-920075	19950523
EP 760683	B1	20000105		
R: DE, FR, GB, IT				

JP 10501528	T2	19980210	JP 1995-500267	19950523
NO 9604967	A	19970123	NO 1996-4967	19961122
PRIORITY APPLN. INFO.:			IT 1994-MI1074	19940526
			WO 1995-EP1958	19950523

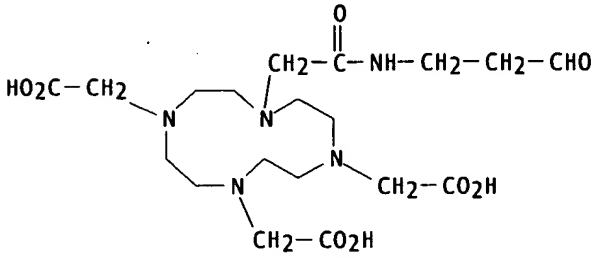
OTHER SOURCE(S): MARPAT 124:192411

AB The invention relates to novel paramagnetic metal ion chelates and their use as contrast agents in the diagnostic technique known as magnetic resonance imaging (M.R.I.). In particular, the prepn. of gadolinium complexes of cholic acid diethylenetriaminopentaacetatic acid or 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetatic acid deriv. conjugates with meglumine is described.

IT **174267-53-9P 174267-54-0P 174267-80-2P**
174267-83-5P 174267-87-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(for prepn. of gadolinium complexes with cholic acid diethylenetriaminopentaacetate or tetraazacyclododecanetetraacetate derivs. as MRI imaging agents)

RN 174267-53-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-[(3-oxopropyl)amino]ethyl]- (9CI) (CA INDEX NAME)

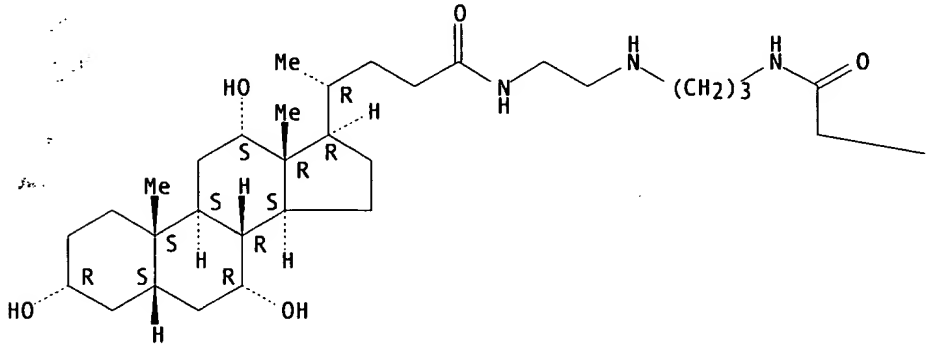


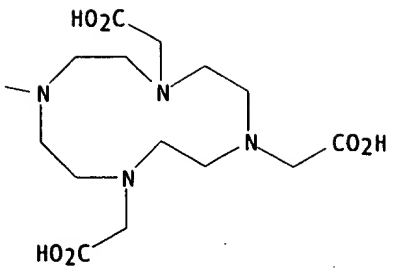
RN 174267-54-0 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-[[3-[[2-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]ethyl]amino]propyl]amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

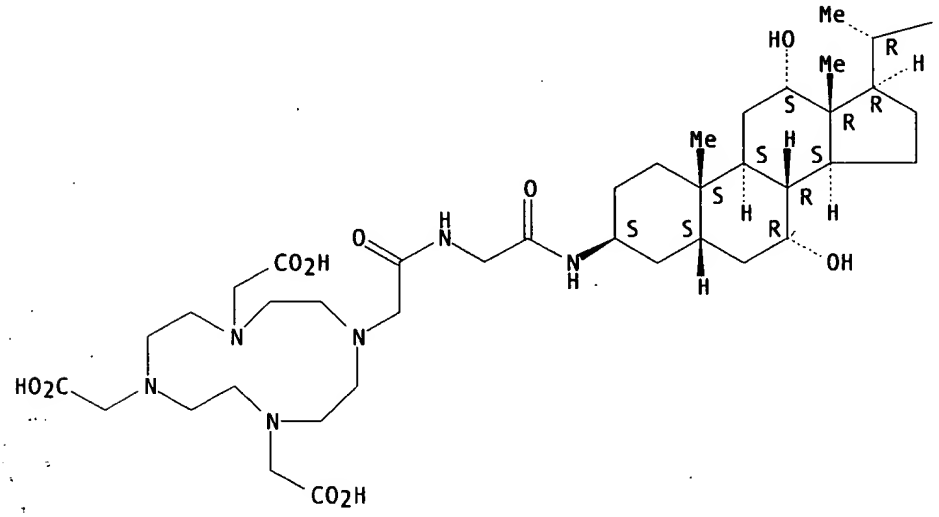
PAGE 1-A

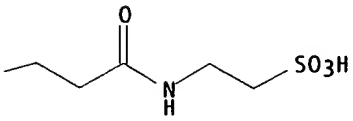




RN 174267-80-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[(3.beta.,5.beta.,7.alpha.,12.alpha.)-7,12-dihydroxy-24-oxo-24-[(2-sulfoethyl)amino]cholan-3-yl]amino]-2-oxoethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

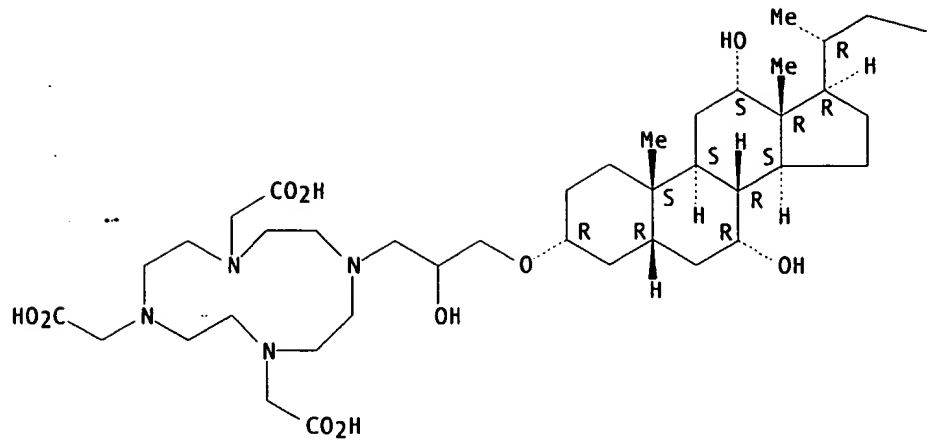




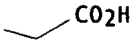
RN 174267-83-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-23-carboxy-7,12-dihydroxy-24-norcholan-3-yl]oxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



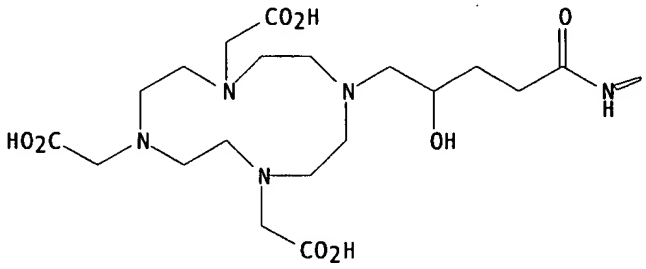
PAGE 1-B



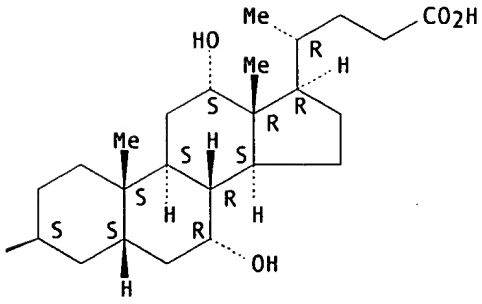
RN 174267-87-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[5-[[(3.beta.,5.beta.,7.alpha.,12.alpha.)-23-carboxy-7,12-dihydroxy-24-norcholan-3-yl]amino]-2-hydroxy-5-oxopentyl]- (9CI) (CA INDEX NAME)

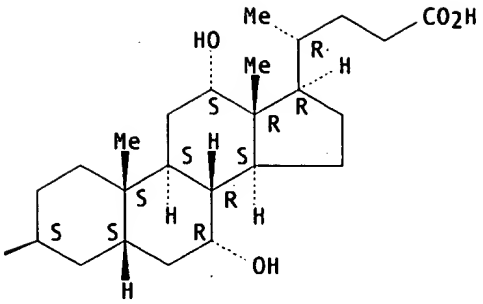
Absolute stereochemistry.

PAGE 1-A



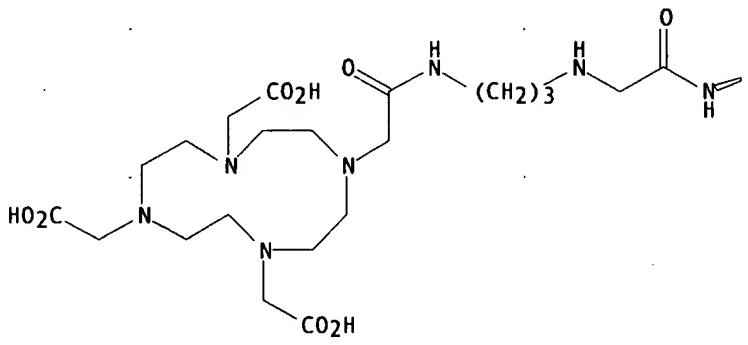
PAGE 1-B

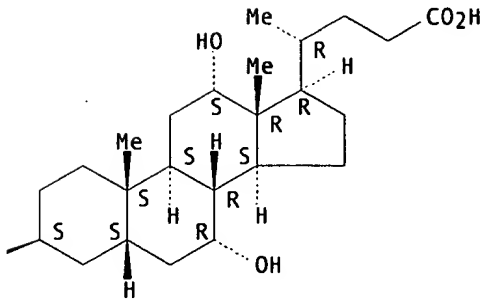




IT 174267-88-0P 174267-94-8P 174268-01-0P
174268-02-1P 174268-03-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. as chelating ligands for MRI imaging agents)
RN 174267-88-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-[[2-[[(3.beta.,5.beta.,7.alpha.,12.alpha.)-23-carboxy-7,12-dihydroxy-24-norcholan-3-yl]amino]-2-oxoethyl]amino]propyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



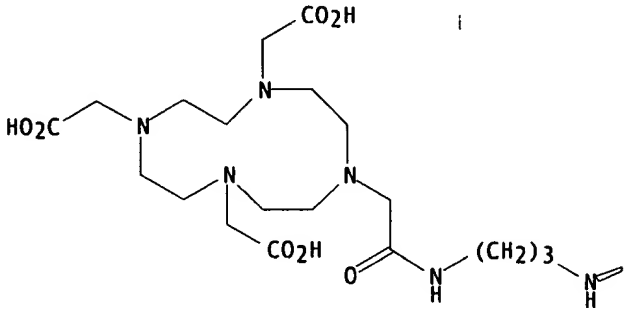


RN 174267-94-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[3-

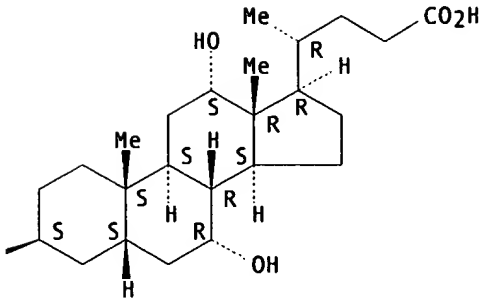
[[(3.beta.,5.beta.,7.alpha.,12.alpha.)-23-carboxy-7,12-dihydroxy-24-norcholan-3-yl]amino]propyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

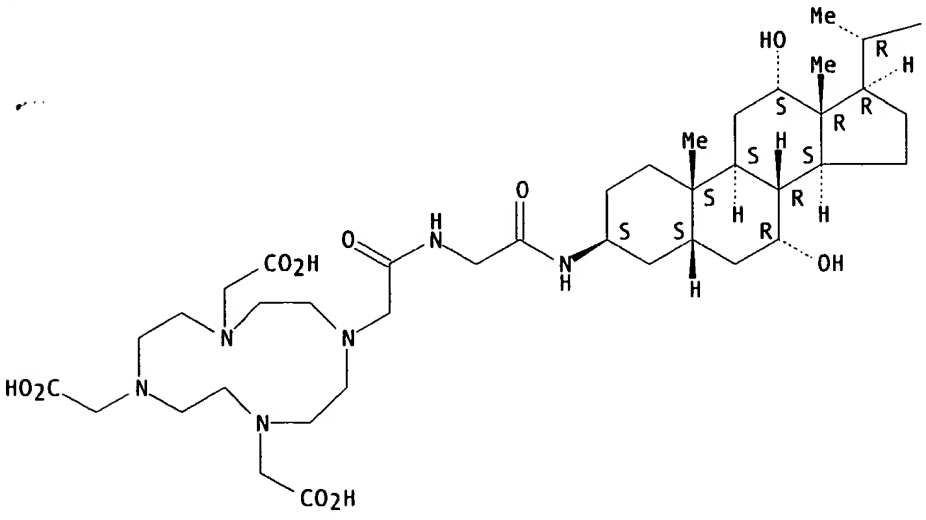


RN 174268-01-0 CAPLUS

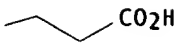
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[[(3.beta.,5.beta.,7.alpha.,12.alpha.)-23-carboxy-7,12-dihydroxy-24-norcholan-3-yl]amino]-2-oxoethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



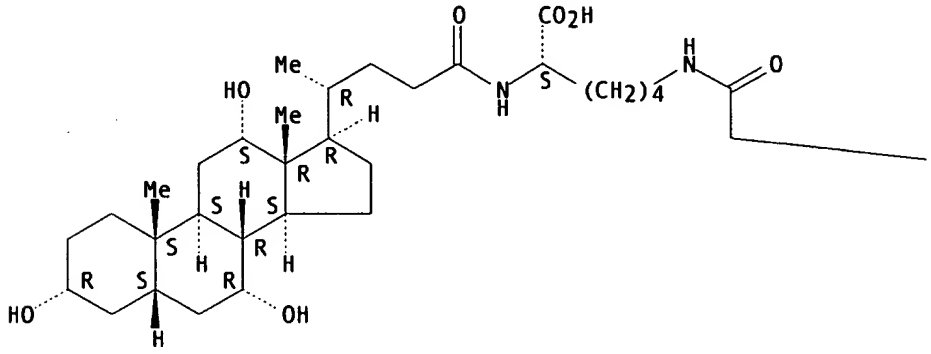
PAGE 1-B



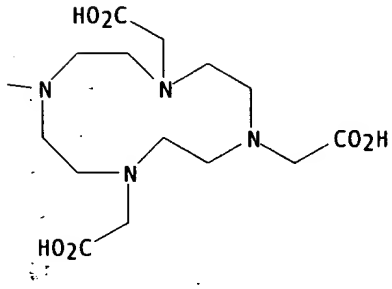
RN 174268-02-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[5-carboxy-5-[[(3.alpha.,5.beta.,7.alpha.,12.alpha.)-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]pentyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

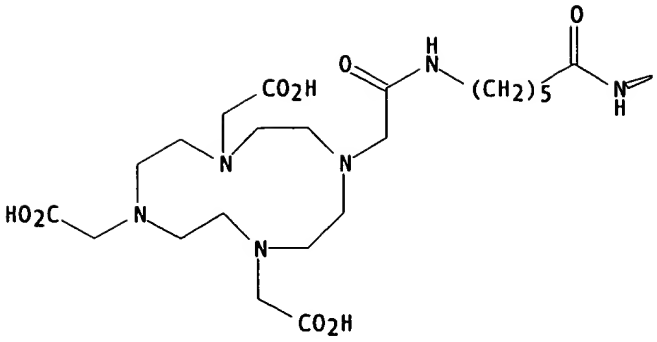


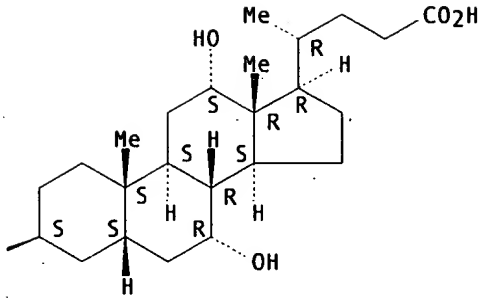
PAGE 1-B



RN 174268-03-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[(3.beta.,5.beta.,7.alpha.,12.alpha.)-23-carboxy-7,12-dihydroxy-24-norcholan-3-yl]amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L10 ANSWER 52 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:998375 CAPLUS
DOCUMENT NUMBER: 124:202320
TITLE: Preparation of dendrimers linked to drug or diagnostic agents.
INVENTOR(S): Margerum, Larry; Campion, Brian; Fellman, Jere Douglas; Garrity, Martha
PATENT ASSIGNEE(S): Nycomed Imaging AS, Norway; Cockbain, Julian
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

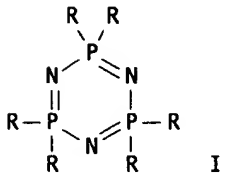
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528966	A1	19951102	WO 1995-GB898	19950420
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2187921	AA	19951102	CA 1995-2187921	19950420
AU 9522631	A1	19951116	AU 1995-22631	19950420
EP 756496	A1	19970205	EP 1995-915939	19950420

R: DE, ES, FR, GB, IE, IT

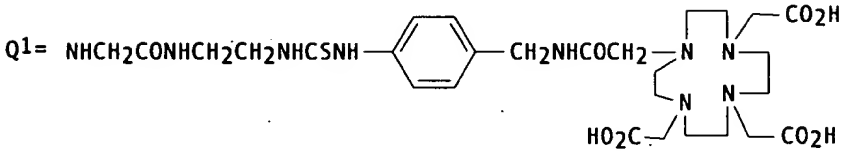
CN 1150391	A	19970521	CN 1995-193094	19950420
JP 09512264	T2	19971209	JP 1995-527454	19950420
US 5834020	A	19981110	US 1997-722082	19970121
PRIORITY APPLN. INFO.:			GB 1994-7812	19940420
			WO 1995-GB898	19950420

OTHER SOURCE(S): MARPAT 124:202320

GI



I



AB Dendrimeric compds. comprising a dendrimeric backbone linked to a plurality of diagnostically or therapeutically active moieties, characterized in that the mol. skeleton of said compd. contains .gtoreq.1 biodegradable cleavage site such that on cleavage the active moieties are released in renally excretable form, were prepd. Thus, the Gd chelate of phosphazene (I; R = Q1) was prepd. and its hydrolysis by mouse liver enzymes was studied.

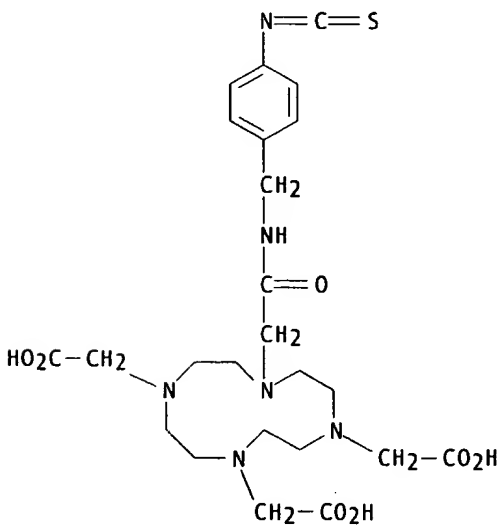
IT **174131-79-4**
RL: RCT (Reactant)
(dendritic; prepn. of dendrimers linked to drug or diagnostic agents)

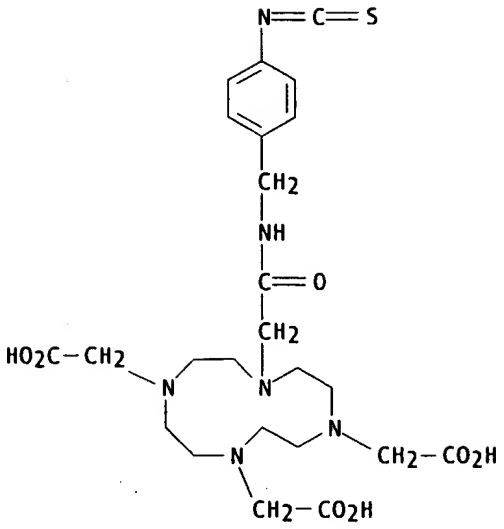
RN 174131-79-4 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-isothiocyanatophenyl)methyl]amino]-2-oxoethyl]-, polymer with 1,2-ethanediamine (9CI) (CA INDEX NAME)

CM 1

CRN 174131-78-3
CMF C24 H34 N6 O7 S



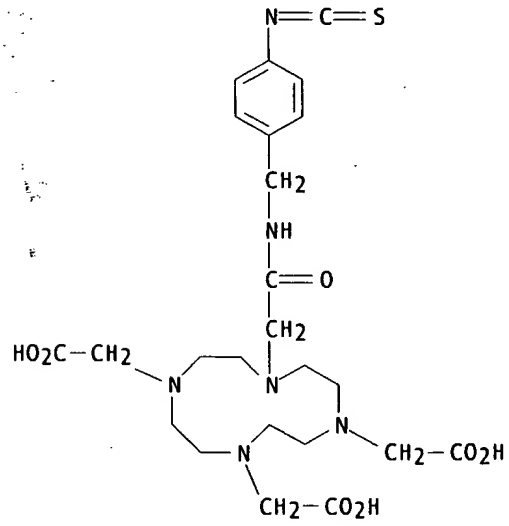


CM 2

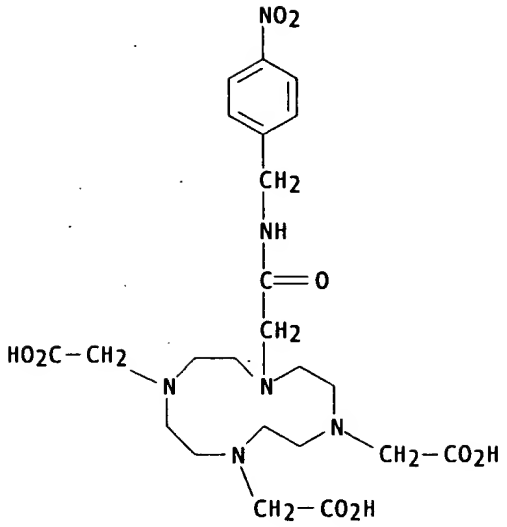
CRN 107-15-3
CMF C2 H8 N2

$H_2N-CH_2-CH_2-NH_2$

IT 174131-78-3
RL: RCT (Reactant)
(prepn. of dendrimers linked to drug or diagnostic agents)
RN 174131-78-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-isothiocyanatophenyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



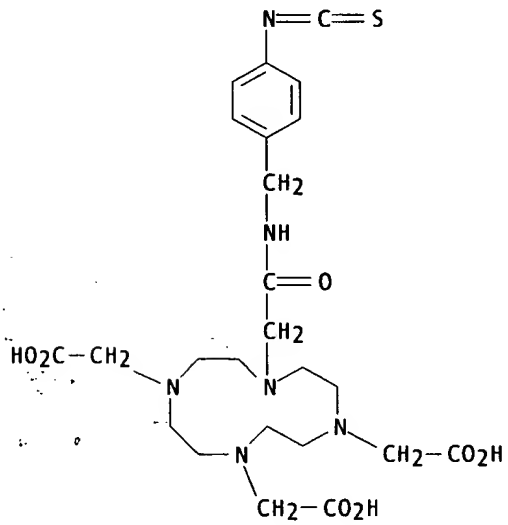
IT 174131-72-7P 174131-79-4DP, Gadolinium complex
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of dendrimers linked to drug or diagnostic agents)
RN 174131-72-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-nitrophenyl)methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 174131-79-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[(4-isothiocyanatophenyl)methyl]amino]-2-oxoethyl]-, polymer with 1,2-ethanediamine (9CI) (CA INDEX NAME)

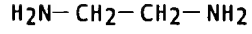
CM 1

CRN 174131-78-3
CMF C24 H34 N6 O7 S



CM 2

CRN 107-15-3
CMF C2 H8 N2



L10 ANSWER 53 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:998374 CAPLUS
DOCUMENT NUMBER: 124:139993
TITLE: Gadolinium complexes as contrast agents
INVENTOR(S): Margerum, Larry; Campion, Brian; Fellmann, Jere

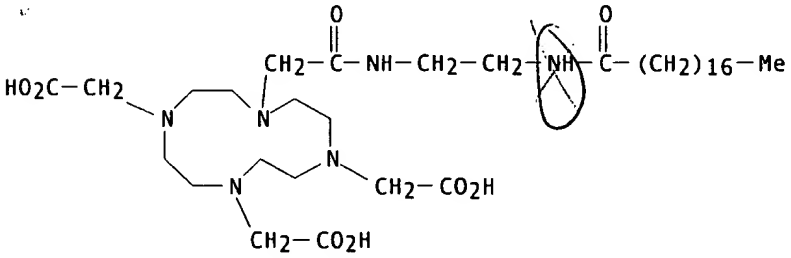
Douglas; Garrity, Martha; Varadarajan, John
PATENT ASSIGNEE(S): Nycomed Imaging AS, Norway; Cockbain, Julian
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528967	A1	19951102	WO 1995-GB899	19950420
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2188292	AA	19951102	CA 1995-2188292	19950420
AU 9522632	A1	19951116	AU 1995-22632	19950420
EP 755269	A1	19970129	EP 1995-915940	19950420
R: DE, ES, FR, GB, IE, IT				
CN 1148813	A	19970430	CN 1995-193198	19950420
JP 09512265	T2	19971209	JP 1995-527455	19950420
PRIORITY APPLN. INFO.:			GB 1994-7812	19940420
			GB 1994-20657	19941013
			WO 1995-GB899	19950420

AB A blood pool contrast agent having an overall mol. wt. of at least 10KD comprising a macrostructure which is bound to a plurality of opsonization-inhibiting moieties is described, which carries chelated ionic paramagnetic or heavy metal moieties, the chelating groups being macrocyclic and the macrostructure is liposomal. Gd(III) complexes were prepd. by treatment of 1,4,7,10-tetraazacyclododecane deriv. with Gd(III). Liposomes contg. the complex were administered to rats and the biodistribution was the highest in the liver.

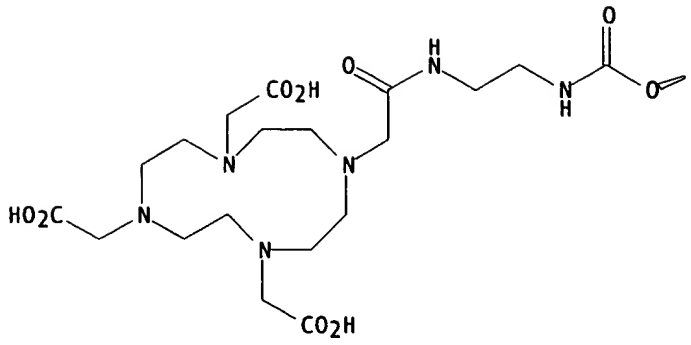
IT **173308-27-5P 173308-28-6P**
RL: BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(prepn. of gadolinium complexes as contrast agents)

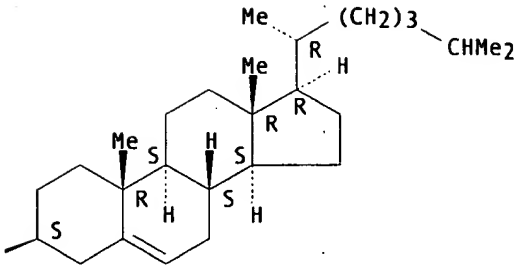
RN 173308-27-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-[[2-[(1-oxooctadecyl)amino]ethyl]amino]ethyl]- (9CI) (CA INDEX NAME)



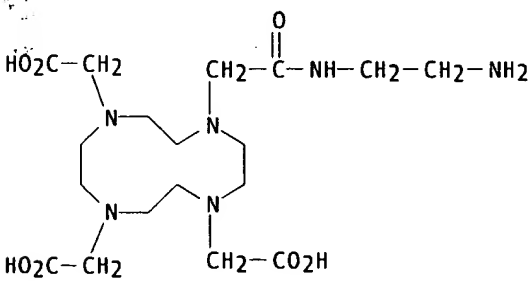
RN 173308-28-6 CAPLUS
CN Cholest-5-en-3-ol (3.beta.)-, [2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

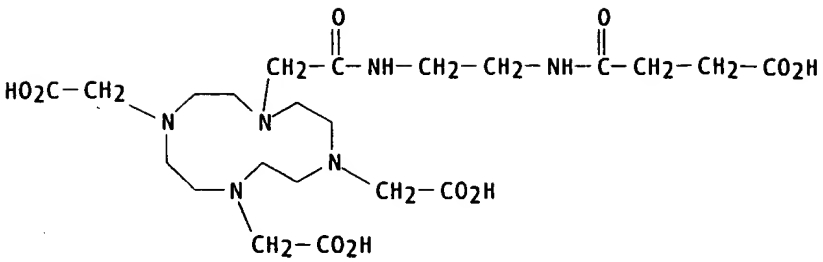




IT 150467-20-2P 173308-24-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of gadolinium complexes as contrast agents)
RN 150467-20-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 173308-24-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-[(3-carboxy-1-oxopropyl)amino]ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 54 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:995412 CAPLUS
DOCUMENT NUMBER: 124:49701
TITLE: Method for preparing radionuclide-labeled chelating agent-ligand complexes
INVENTOR(S): Meares, Claude F.; Li, Min; DeNardo, Sally J.
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9526206	A1	19951005	WO 1995-US3722	19950323
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9521946	A1	19951017	AU 1995-21946	19950323
US 5958374	A	19990928	US 1996-767702	19961217
PRIORITY APPLN. INFO.:			US 1994-218591	19940328
			WO 1995-US3722	19950323

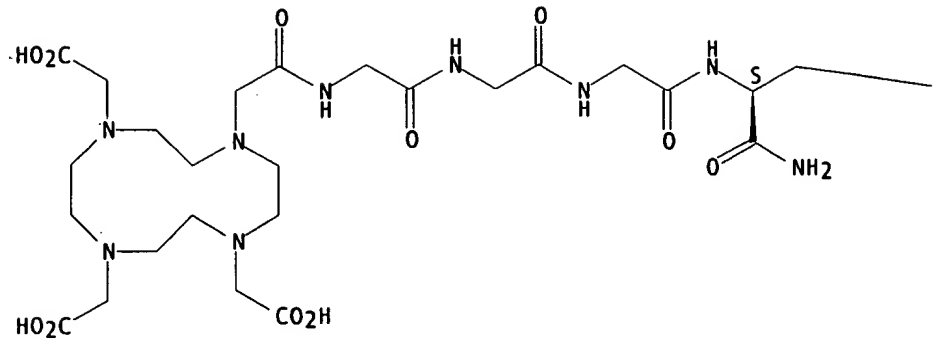
AB Radionuclide-labeled chelating agent-ligand complexes that are useful in medical diagnosis or therapy are prepd. by reacting a radionuclide, such as 90Y or 111In, with a polyfunctional chelating agent to form a radionuclide chelate that is elec. neutral; purifying the chelate by anion-exchange chromatog.; and reacting the purified chelate with a targeting mol., e.g. a monoclonal antibody, to form the complex. The prelabeling methodol. of the invention was used to prep. and purify complexes of 90Y and 111In with 1,4,7,10-tetraazacyclododecane-N-[Gly3(L-(p-isothiocyanato)-Phe-amide)acetyl]-N',N'',N'''-triacetic acid; the resulting chelates were conjugated with a monoclonal antibody. Biodistribution of the 90Y-labeled conjugate was detd.

IT 149206-88-2
RL: RCT (Reactant)
(radionuclide-labeled chelating agent-ligand complex prepn. using radionuclide prelabeling and anion-exchange chromatog.)

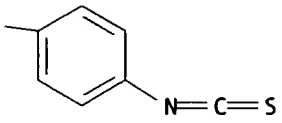
RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



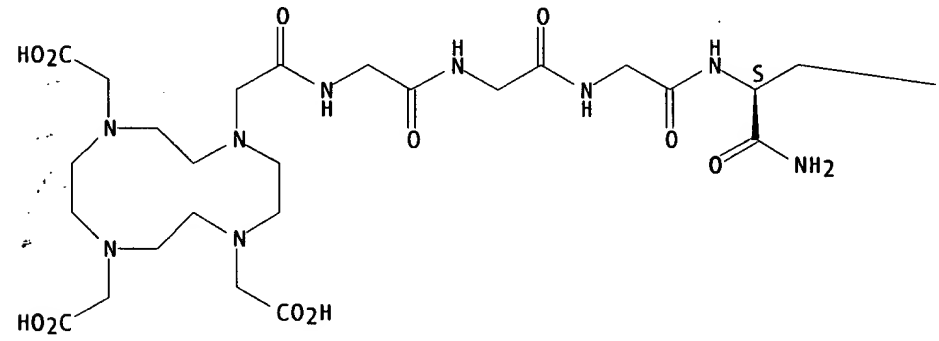
PAGE 1-B



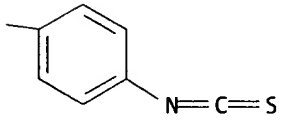
IT **149206-88-2D**, reaction products with 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(radionuclide-labeled chelating agent-ligand complex prepn. using radionuclide prelabeling and anion-exchange chromatog.)
RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

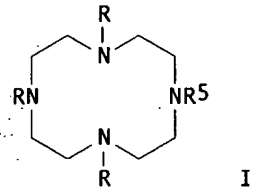


L10 ANSWER 55 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:913276 CAPLUS

DOCUMENT NUMBER: 123:314032
TITLE: Preparation of N-(sulfonamidoalkyl)-1,4,7,10-tetraazacyclododecanes as chelants for diagnostic and therapeutic metal complexes
INVENTOR(S): Hilger, Christoph-Stephan; Ebert, Wolfgang; Lee-Vaupel, Mary; Platzek, Johannes; Conrad, Juergen; Raduechel, Bernd
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4340809	A1	19950601	DE 1993-4340809	19931124
DE 4340809	C2	20000803		
CA 2177271	AA	19950601	CA 1994-2177271	19941110
WO 9514678	A1	19950601	WO 1994-EP3718	19941110
W: AU, CA, JP, KR, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9481073	A1	19950613	AU 1994-81073	19941110
EP 730586	A1	19960911	EP 1995-900135	19941110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09505313	T2	19970527	JP 1994-514789	19941110
ZA 9409347	A	19950810	ZA 1994-9347	19941124
US 5919431	A	19990706	US 1996-649672	19961206
PRIORITY APPLN. INFO.:			DE 1993-4340809	19931124
			WO 1994-EP3718	19941110

OTHER SOURCE(S): MARPAT 123:314032
GI

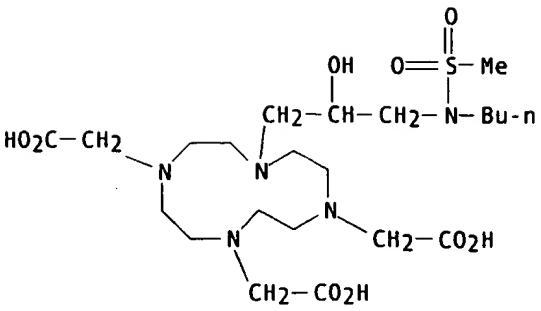


I

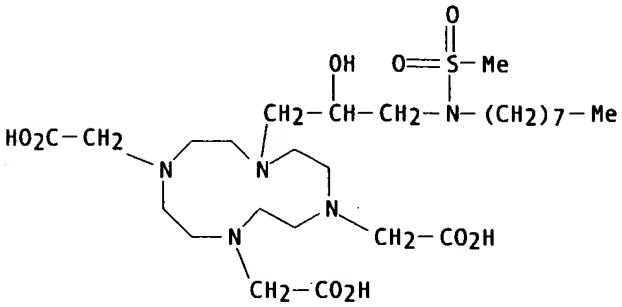
AB Title compds. [I; R = CHR2CO2R1; R1 = H, alkyl, neg. charge; R2 = H, Me, Et; R5 = CH2XNR3SO2R4; R3 = H, (un)substituted alk(en)yl, -aryl(alkyl), etc.; R4 = (un)substituted alk(en)yl, -aryl(alkyl), etc.; R3R4 = atoms to complete a ring; X = (hydroxy- or alkoxy-substituted)(O- or CO-interrupted)alkylene] were prepd. as ligands for diagnostic and therapeutic metal complexes (no data). Thus, I (R = CH2CO2R6)(II; R5 = R6 = H) was condensed with N-octyl-N-glycidylmethanesulfonamide (prepn. described) to give, after sapon. and complexation, II.Ga [R = CH2CO2-, R5 = CH2CH(OH)CH2NR3SO2Me, R3 = octyl].

IT **170215-80-2P 170215-82-4P 170215-84-6P**
170215-86-8P 170215-88-0P 170215-90-4P
170215-92-6P 170215-94-8P 170215-96-0P
170215-98-2P 170216-00-9P 170216-02-1P
170216-05-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-(sulfonamidoalkyl)-1,4,7,10-tetraazacyclododecanes as chelants for diagnostic and therapeutic metal complexes)

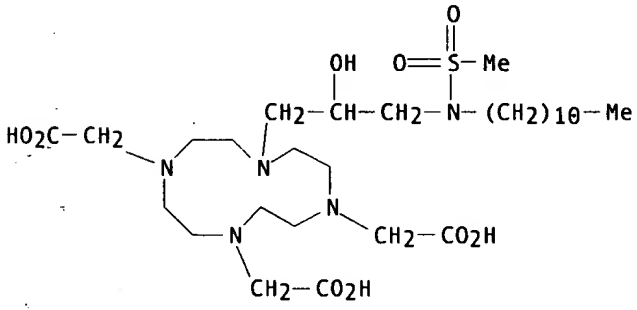
RN 170215-80-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[butyl(methylsulfonyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



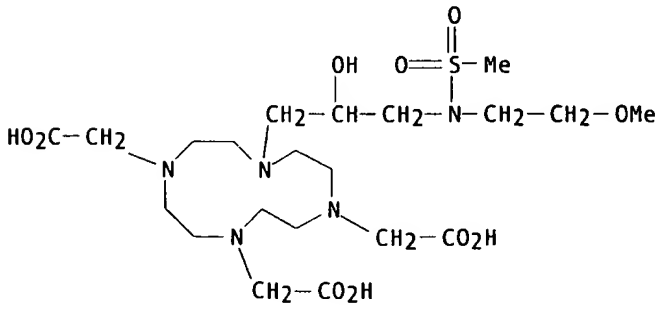
RN 170215-82-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(methylsulfonyl)octylamino]propyl]- (9CI) (CA INDEX NAME)



RN 170215-84-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(methylsulfonyl)undecylamino]propyl]- (9CI) (CA INDEX NAME)

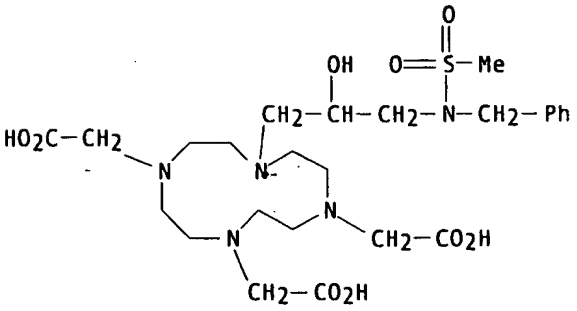


RN 170215-86-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(2-methoxyethyl)(methylsulfonyl)amino]propyl]- (9CI) (CA INDEX NAME)

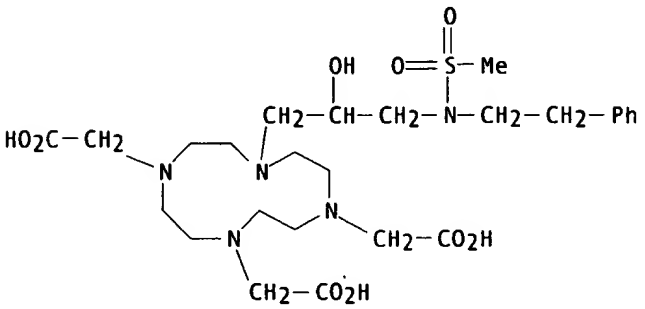


RN 170215-88-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-

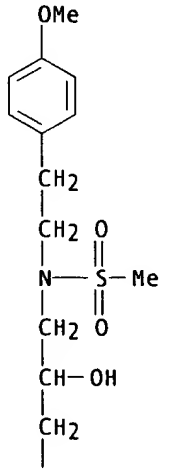
[(methylsulfonyl)(phenylmethyl)amino]propyl]- (9CI) (CA INDEX NAME)

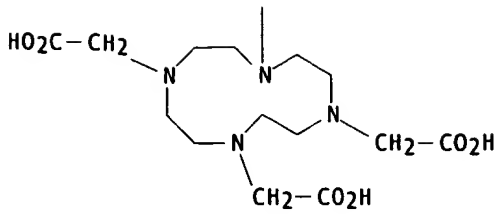


RN 170215-90-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(methylsulfonyl)(2-phenylethyl)amino]propyl]- (9CI) (CA INDEX NAME)

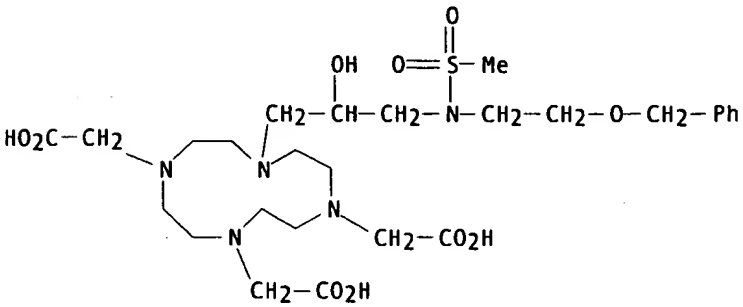


RN 170215-92-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[[2-(4-methoxyphenyl)ethyl](methylsulfonyl)amino]propyl]- (9CI) (CA INDEX NAME)

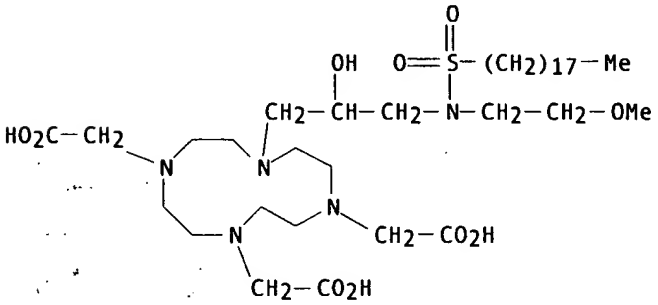




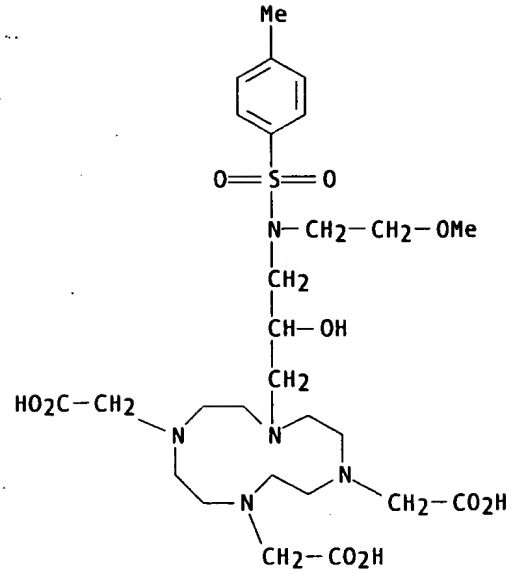
RN 170215-94-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(methylsulfonyl)[2-(phenylmethoxy)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)



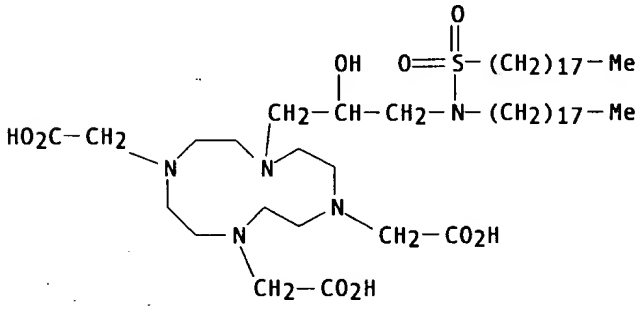
RN 170215-96-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(2-methoxyethyl)(octadecylsulfonyl)amino]propyl]- (9CI) (CA INDEX NAME)



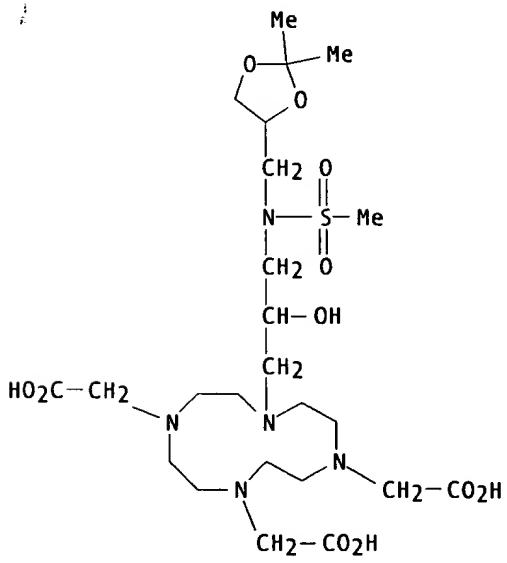
RN 170215-98-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(2-methoxyethyl)[(4-methylphenyl)sulfonyl]amino]propyl]- (9CI) (CA INDEX NAME)



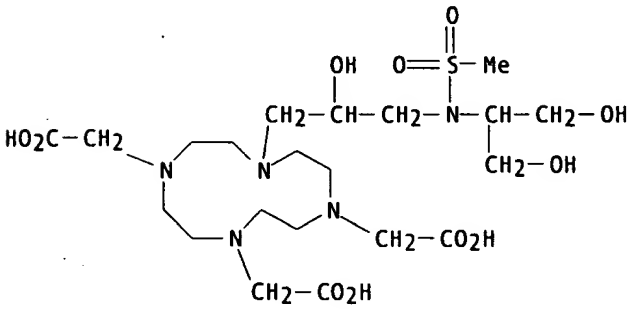
RN 170216-00-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[octadecyl(octadecylsulfonyl)amino]propyl]- (9CI) (CA INDEX NAME)



RN 170216-02-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl](methylsulfonyl)amino]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



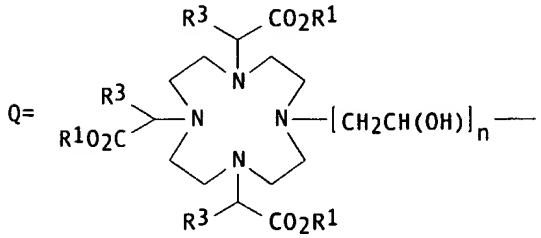
RN 170216-05-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[[2-hydroxy-1-(hydroxymethyl)ethyl](methylsulfonyl)amino]propyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 56 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:810385 CAPLUS
DOCUMENT NUMBER: 123:228230
TITLE: Preparation of N,N,N-tricarboxymethyl-1,4,7-10-tetraazacyclododecane metal complexes as NMR diagnostic temperature probes
INVENTOR(S): Platzek, Johannes; Raduechel, Bernd; Niedballa, Ulrich; Weinmann, Hanns-Joachim; Bauer, Hans; Roth, Klaus
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427977	A1	19941208	WO 1994-EP1376	19940429
W: CA, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 4318369	C1	19950209	DE 1993-4318369	19930528
EP 700392	A1	19960313	EP 1994-915565	19940429
EP 700392	B1	19981209		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08511247	T2	19961126	JP 1994-500147	19940429
AT 174331	E	19981215	AT 1994-915565	19940429
NO 9504830	A	19951128	NO 1995-4830	19951128
PRIORITY APPLN. INFO.:			DE 1993-4318369	19930528
			WO 1994-EP1376	19940429

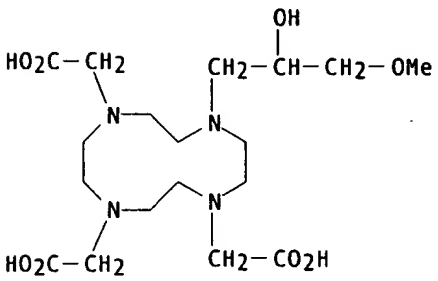
OTHER SOURCE(S): MARPAT 123:228230
GI



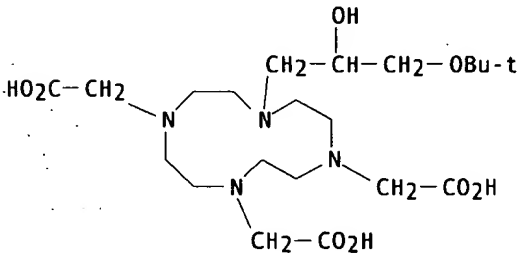
AB RZA [R = tetraazacyclododecyl(hydroxyethyl) group Q; A = H or Q; R1 = H, metal ion; R3 = H, (un)substituted alkyl; Z = (O- or CO-interrupted) (un)substituted alkylene; n = 0 or 1] were prepd. Thus, QH (R1 = R3 = H, n = 0) was N-alkylated by MeOCH2CH2Br to give QCH2CH2OMe (R1 = R3 = H, n = 0) which was stirred 5h at 85.degree. with Pr2O3 in water to give the Pr complex. The latter was administered i.v. to rats and variation of chem. shift with body temp. data were given.

IT **136687-96-2P 168078-12-4P 168078-27-1P 168078-31-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N,N,N-tricarboxymethyl-1,4,7-10-tetraazacyclododecane metal complexes as NMR diagnostic temp. probes)

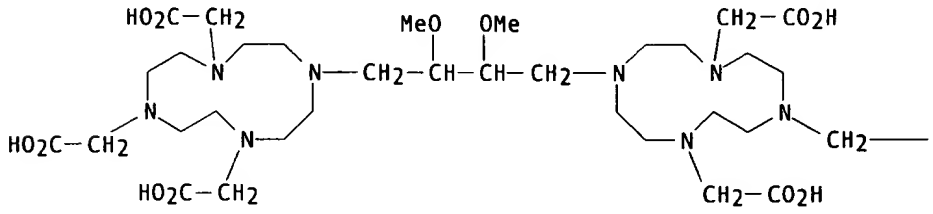
RN 136687-96-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-3-methoxypropyl)- (9CI) (CA INDEX NAME)



RN 168078-12-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-(1,1-dimethylethoxy)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 168078-27-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(2,3-dimethoxy-1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



—CO_2H

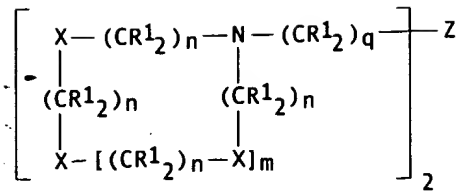
RN 168078-31-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[oxybis(2-methoxy-3,1-propanediyl)]bis- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

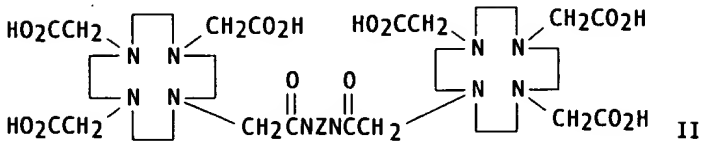
L10 ANSWER 57 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:780306 CAPLUS
DOCUMENT NUMBER: 123:186921
TITLE: Polyazacycloalkanes as dichelants
INVENTOR(S): Carvalho, Joan; Fellmann, Jere Douglas; Watson, Alan David; Koo, Michael
PATENT ASSIGNEE(S): Nycomed Salutar, Inc., USA; Cockbain, Julian Roderic Michaelson
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9509848	A2	19950413	WO 1994-GB2115	19940929
WO 9509848	A3	19950727		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5281704	A	19940125	US 1990-468107	19900119
JP 2000136174	A2	20000516	JP 1999-192219	19901020
US 5446145	A	19950829	US 1993-86996	19930707
CA 2172735	AA	19950413	CA 1994-2172735	19940929
AU 9477042	A1	19950501	AU 1994-77042	19940929
AU 678603	B2	19970605		
EP 722442	A1	19960724	EP 1994-927742	19940929
R: DE, DK, ES, FR, IE, IT				
CN 1136313	A	19961120	CN 1994-194300	19940929
CN 1045772	B	19991020		
HU 74592	A2	19970128	HU 1996-805	19940929
JP 09503500	T2	19970408	JP 1994-510671	19940929
PRIORITY APPLN. INFO.:			US 1990-468107	19900119
			US 1992-855028	19920612
			US 1993-86996	19930707
			GB 1993-20277	19931001
			GB 1989-23843	19891023
			JP 1990-515144	19901020
			WO 1994-GB2115	19940929

OTHER SOURCE(S): MARPAT 123:186921
GI



I



II

AB I (X same or different NZ, O or S, at least two Xs being NZ; each Z is a group R1 or a group CR12Y, at least one Z, and preferably 2 or 3 Zs, on each macrocyclic ring being a group CR12Y; each Y is a group CO2H, PO3H, SO3H, CONR12, CON(OR1)R1, CNS or CONR1NR12, preferably COOH; m is 0 or 1 or 2, preferably 1; each n is 2 or 3, preferably 2; q is 1 or 2, preferably 1; each R1 which may be the same or different is a H atom or an alkyl group optionally substituted by one or more hydroxy and/or alkoxy groups; and D is a bridging group, other than an unsubstituted carbonylaminoethylaminocarbonyl group, having a mol. wt. of <1000, preferably <500, joining two macrocyclic rings via at least one amide or ester bond) and salts and metal chelates were prepd. Thus I (Z = org. radicals) and their Gd or Dy dinuclear complexes were prepd. The Gd complexes were tested a MRI imaging agents.

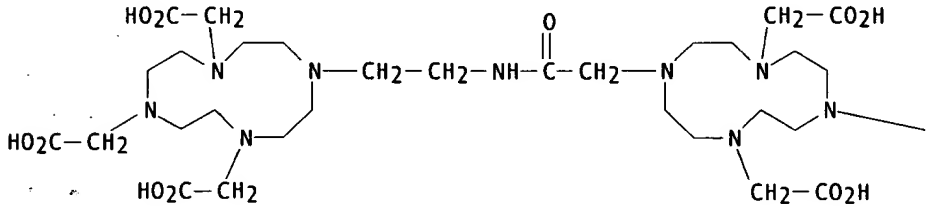
IT **167407-80-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with dysprosium and gadolinium)

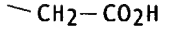
RN 167407-80-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



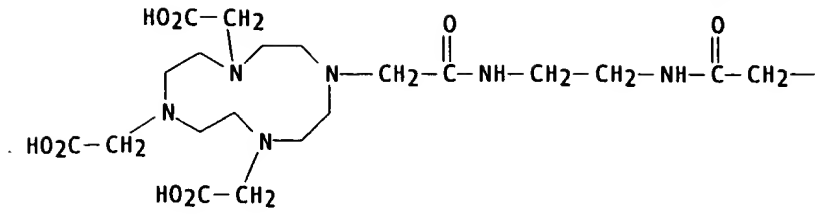
IT **137097-99-5P 167407-69-4P 167407-72-9P**
167407-73-0P 167407-74-1P 167407-75-2P
167407-76-3P 167407-77-4P 167407-78-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with gadolinium)

RN 137097-99-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[imino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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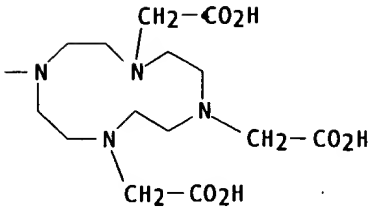
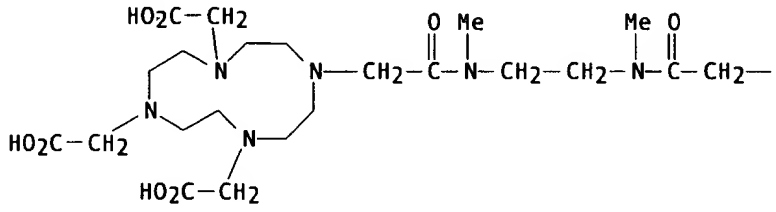
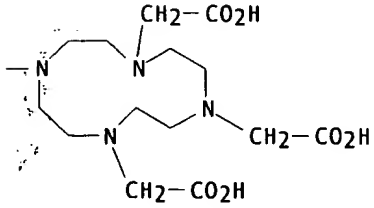


RN 167407-69-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[(methylimino)(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

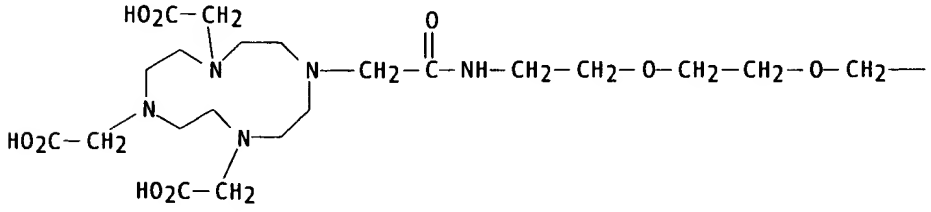


PAGE 1-B

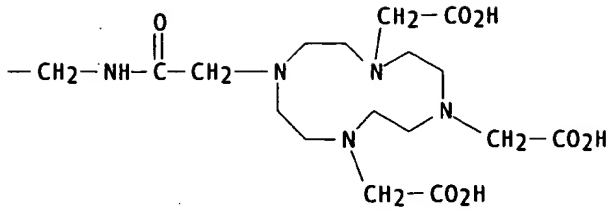


RN 167407-72-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(2,13-dioxo-6,9-dioxa-3,12-diazatetradecane-1,14-diyl)bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



RN 167407-73-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[[(2,3-dihydroxypropyl)imino](2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

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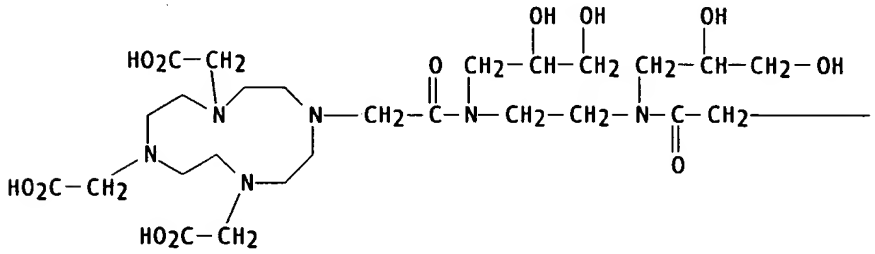
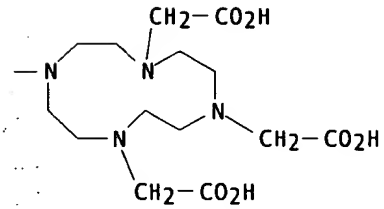


PAGE 1-B



RN 167407-74-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, [1,2-ethanediylbis[[(2-hydroxyethyl)imino](2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

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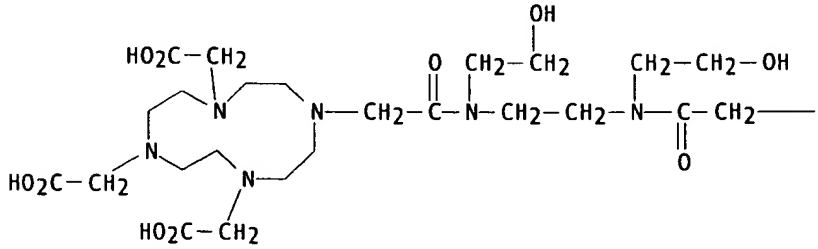
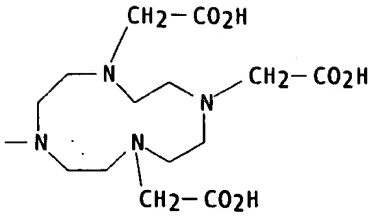


PAGE 1-B



RN 167407-75-2 CAPLUS
CN D-Glucitol, 1-deoxy-1-[methyl[[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl][2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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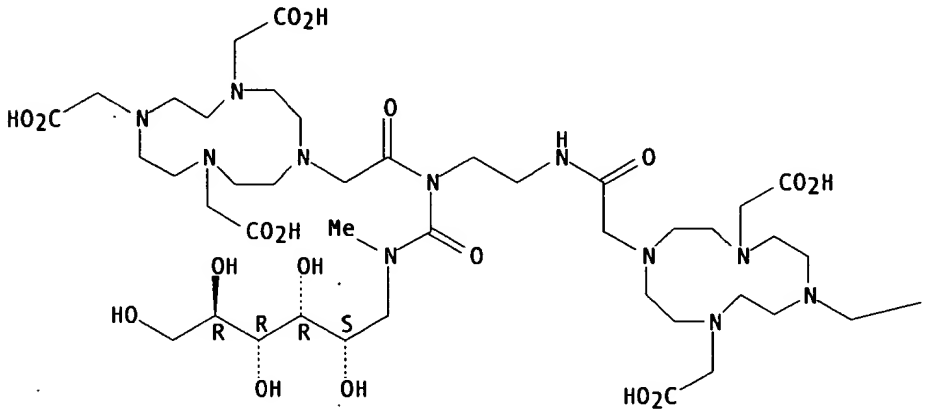
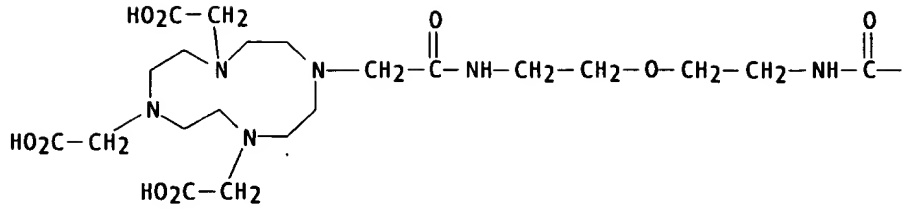


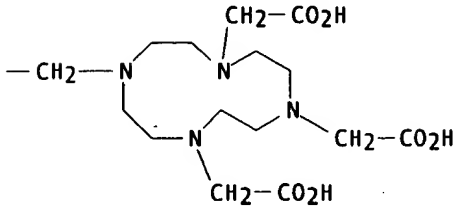
PAGE 1-B

RN 167407-76-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[oxybis[2,1-ethanediylimino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A

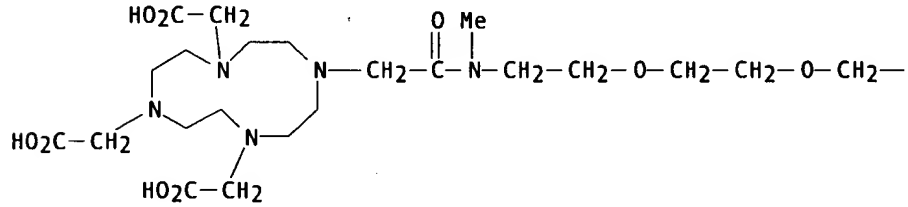


PAGE 1-B



RN 167407-77-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(3,12-dimethyl-2,13-dioxo-6,9-dioxa-3,12-diazatetradecane-1,14-diyl)bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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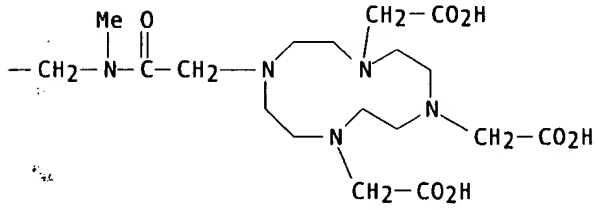
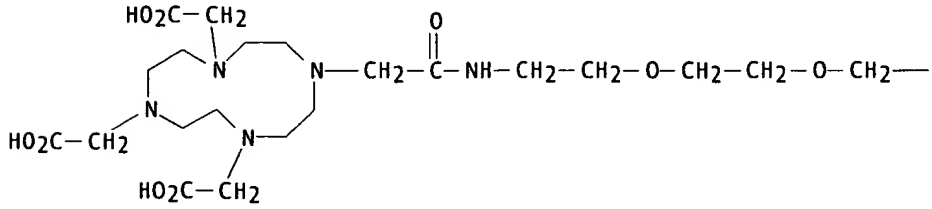
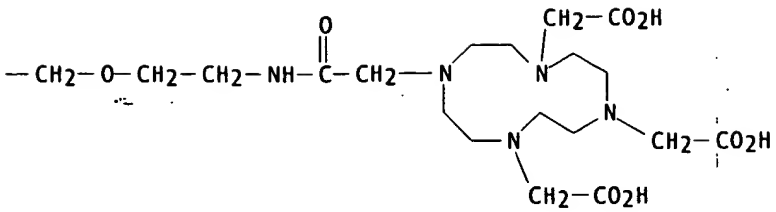


RN 167407-78-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(2,16-dioxo-6,9,12-trioxa-3,15-diazaheptadecane-1,17-diyl)bis- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

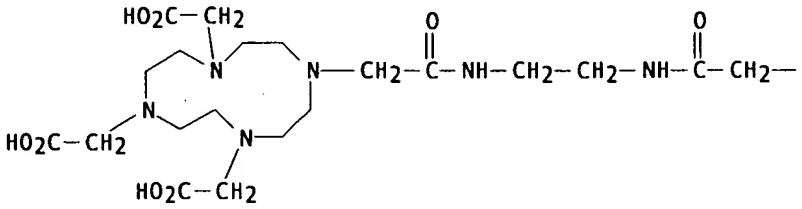


IT 137097-99-5DP, gadolinium complex 167407-69-4DP, gadolinium complex 167407-72-9DP, gadolinium complex 167407-73-0DP, gadolinium complex 167407-74-1DP, gadolinium complex 167407-75-2DP, gadolinium complex 167407-76-3DP, gadolinium complex 167407-77-4DP, gadolinium complex 167407-78-5DP, gadolinium complex 167407-80-9DP, dysprosium and gadolinium complexes
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and use as imaging agent)

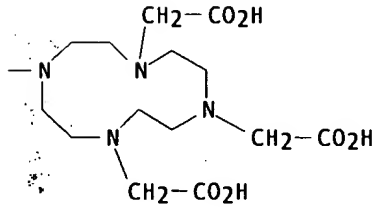
RN 137097-99-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[imino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



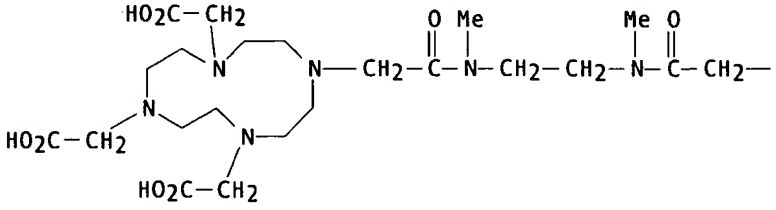
PAGE 1-B



RN 167407-69-4 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[(methylimino)(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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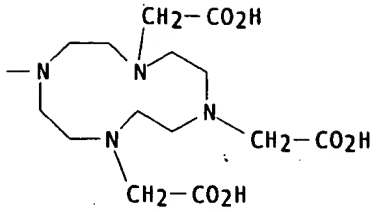

RN 167407-72-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(2,13-dioxo-6,9-dioxa-3,12-diazatetradecane-1,14-diyl)bis- (9CI) (CA INDEX NAME)

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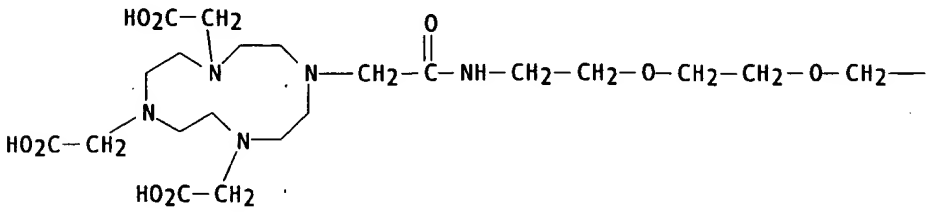
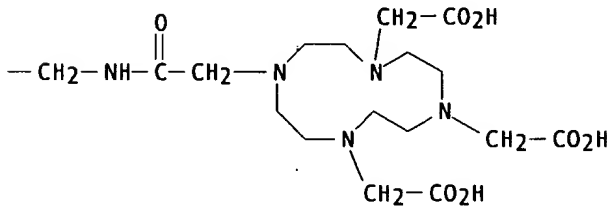
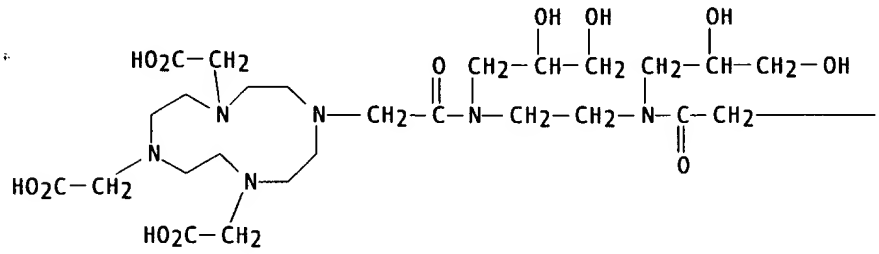


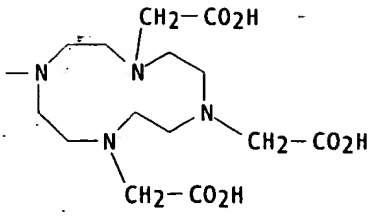
PAGE 1-B



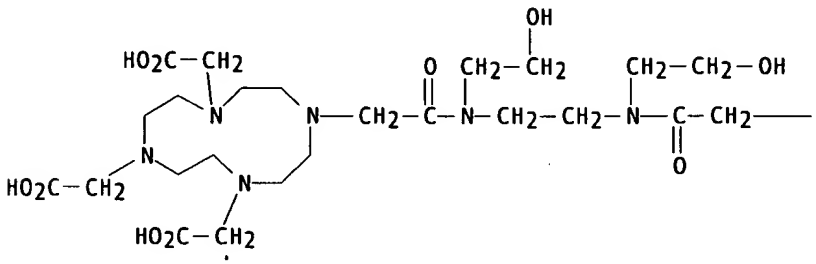
RN 167407-73-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[[(2,3-dihydroxypropyl)imino](2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

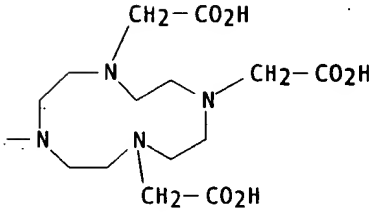
PAGE 1-A





RN 167407-74-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, [1,2-ethanediylbis[[(2-hydroxyethyl)imino](2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

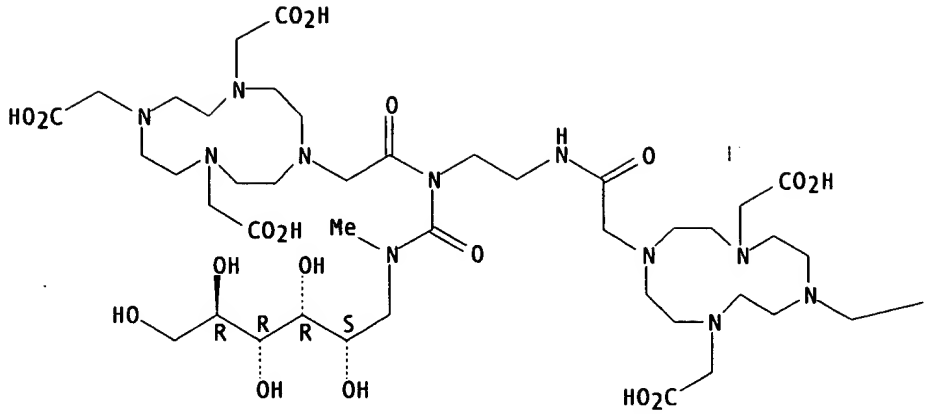




RN 167407-75-2 CAPLUS
CN D-Glucitol, 1-deoxy-1-[methyl[[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl][2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]amino]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

—CO_2H

RN 167407-76-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[oxybis[2,1-ethanediylimino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

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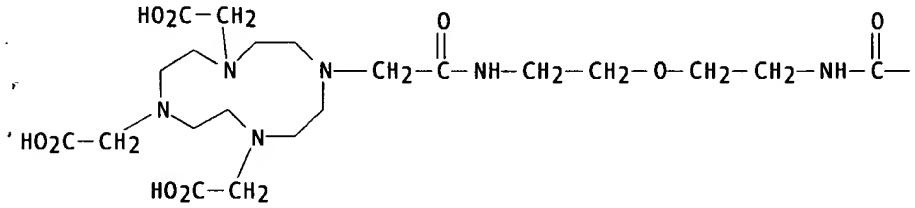
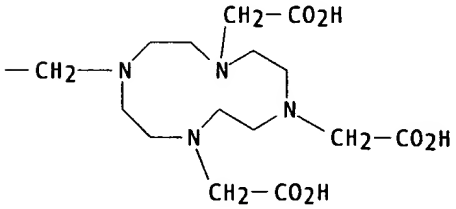


PAGE 1-B



RN 167407-77-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(3,12-dimethyl-2,13-dioxo-6,9-dioxa-3,12-diazatetradecane-1,14-diyl)bis- (9CI) (CA INDEX NAME)

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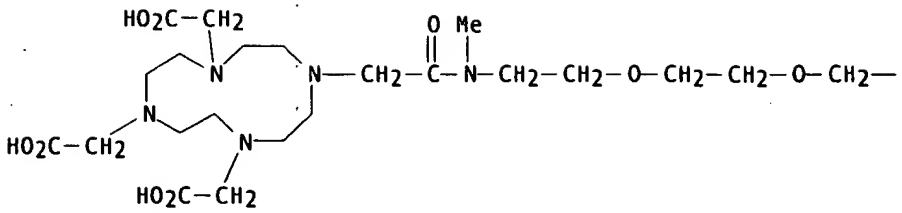
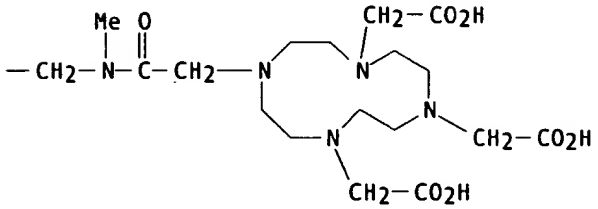
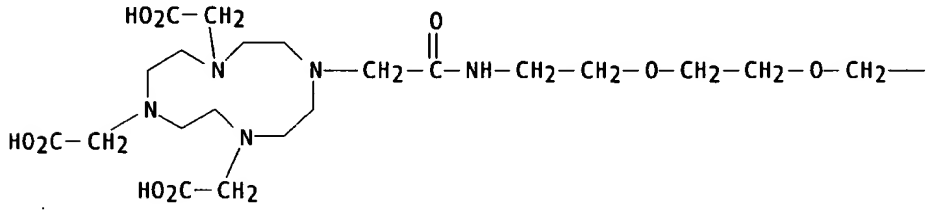


PAGE 1-B



RN 167407-78-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-(2,16-dioxo-6,9,12-trioxa-3,15-diazaheptadecane-1,17-diyl)bis- (9CI) (CA INDEX NAME)

PAGE 1-A



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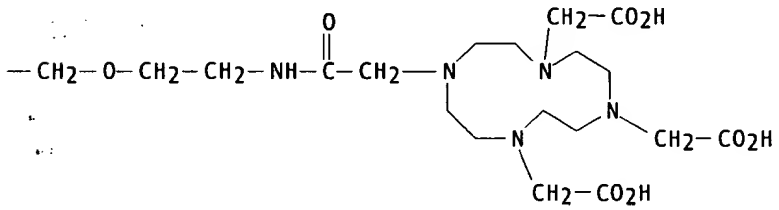

RN 167407-80-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]ethyl]- (9CI) (CA INDEX NAME)

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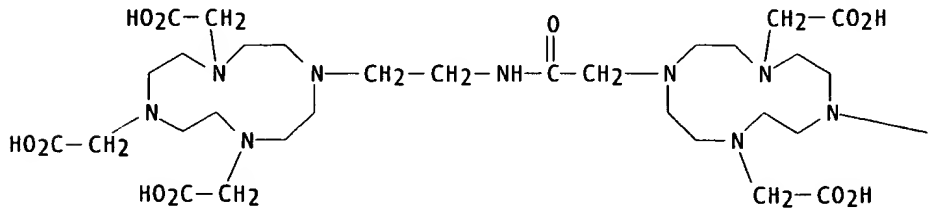
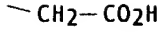




L10 ANSWER 58 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:616058 CAPLUS
DOCUMENT NUMBER: 123:137600
TITLE: Pharmacokinetics of chimeric L6 conjugated to indium-111- and yttrium-90-DOTA-peptide in tumor-bearing mice
AUTHOR(S): DeNardo, Sally J.; Zhong, Gao-Ren; Salako, Qansy; Li, Min; DeNardo, Gerald L.; Meares, Claude F.
CORPORATE SOURCE: Department Internal Medicine, University of California, Davis, CA, USA
SOURCE: J. Nucl. Med. (1995), 36(5), 829-36
CODEN: JNMEAQ; ISSN: 0161-5505
DOCUMENT TYPE: Journal
LANGUAGE: English

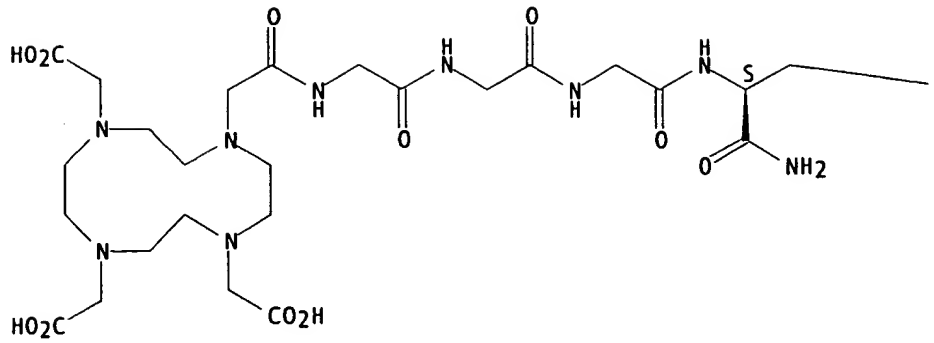
AB A bifunctional chelating agent, DOTA-Gly3-L-(p-isothiocyanato)-phenylalanine amide (DOTA-peptide-NCS), was studied in nude mice bearing human breast cancer xenographs (HBT 3477) to det. its potential for radioimmunoconjugate therapy. Indium-111 and yttrium-90 were attached to an anti-adenocarcinoma chimeric L6 (ChL6) monoclonal antibody (MAb) after pre-chelation to the DOTA-peptide-NCS and the desired neutral radiochelates were obtained by purifn. The unique characteristic of the DOTA-peptide-NCS to form neutral complexes with trivalent metals was utilized to sep. the resulting 111In and 90Y radiochelates from excess chelating agent and other anionic byproducts resulting from metal impurities. The purified radiochelates were then conjugated to ChL6. The pharmacokinetics of 111In- and 90Y-DOTA-peptide-ChL6 were obtained for 5 days after injection in nude mice bearing HBT 3477 xenographs. The results were compared with the pharmacokinetics of 125I-ChL6 obtained in the same mouse model. The whole-body clearance of 125I-ChL6, 90Y- and 111In-DOTA-peptide-ChL6 was monoexponential with biol. half-times of 92, 104 and 160 h, resp. Blood clearances of the three radiopharmaceuticals were biphasic. The radiometal immunoconjugates had greater tumor uptake and slower clearances. Indium-111- and 90Y-DOTA-peptide-ChL6 can be produced at high specific activity with fewer than one chelate per MAb by using a pre-labeling method that permits radiochelate purifn. by charge selection. Studies in mouse xenografts indicate that tumor uptake is enhanced and a favorable therapeutic index is achieved using these agents.

IT **149206-88-2D**, complexes with radionuclides and chimeric L6 monoclonal antibody
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmacokinetics of chimeric L6 conjugated to indium-111- and yttrium-90-DOTA-peptide in tumor-bearing mice)

RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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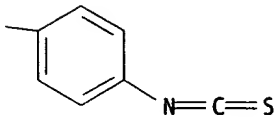


L10 ANSWER 59 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:615003 CAPLUS
DOCUMENT NUMBER: 123:33650
TITLE: Preparation of metal complexes of endothelin analogs and radioiodinated endothelin analogs for diagnosis of cardiovascular disease
INVENTOR(S): Dinkelborg, Ludger; Erber, Sebastian; Hilger, Christoph Stephen; Kramp, Wolfgang; Schier, Hans-Martin; Speck, Ulrich; Gries, Heinz; Platzek, Johannes; Reiser, Joseph H.
PATENT ASSIGNEE(S): Institut fuer Diagnostikforschung GmbH an der Freien Universitaet Berlin, Germany
SOURCE: Ger. Offen., 39 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4301871	A1	19940714	DE 1993-4301871	19930113
EP 606683	A2	19940720	EP 1993-250286	19931022
EP 606683	A3	19951227		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2113245	AA	19940714	CA 1994-2113245	19940111
AU 9453146	A1	19940721	AU 1994-53146	19940112
AU 666059	B2	19960125		
ZA 9400186	A	19940818	ZA 1994-186	19940112
JP 07149799	A2	19950613	JP 1994-2268	19940113

PRIORITY APPLN. INFO.: DE 1993-4301871 19930113

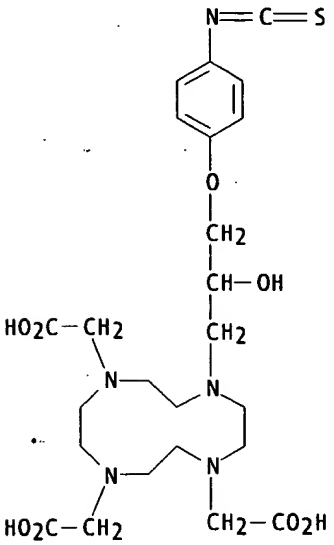
AB Complexes of ELKb with metal ions of at. nos. 21-32, 37-39, 42-51, and 57-83 [E = residue of endothelin, endothelin deriv., endothelin antagonist, etc.; L = bond, Z1RZ2; R = (O-, S-, CO-, NH-, alkylimino-, alkyliminocarbonyl-, NHCO-interrupted) (HO- or epoxy-substituted) alkyl; Z1, Z2 = O, S, CO2, NHCSNH, CO, CSO, etc.; K = chelating residue; b = 0,1], and radioiodoendothelin derivs., were prepd. for diagnosis of cardiovascular disease. Thus, S-benzoylthioacetyl-Gly-Gly-Gly-OH and N-hydroxysuccinimide in DMF at -15.degree. were treated with DCC in DMF; the mixt. was stirred 2 h at -5.degree., 2 h at room temp, and then cooled to -15.degree. and filtered. The filtrate was combined with

H-Gly-Asp-His-Leu-Asp-Ile-Ile-Trp-OH and the mixt. was stirred 20 h at room temp. to give S-benzoylthioacetyl-Gly-Gly-Gly-Gly-Asp-His-Leu-Asp-Ile-Ile-Trp-OH. This was treated with a pertechnate soln. in a citrate buffer to give S-benzoylthioacetyl-Gly-Gly-Gly-Gly-Asp-His-Leu-Asp-Ile-Ile-Trp-OH 99m-Tc complex. 123I-labeled endothelin 1 was prepd. and used to image atherosclerotic changes in rabbit aortas via autoradiog.

IT **163836-51-9**
RL: RCT (Reactant)
(reaction of, in prepn. of peptide analog metal complex for diagnosis of cardiovascular disease)

RN 163836-51-9 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-(4-isothiocyanatophenoxy)propyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 60 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:382753 CAPLUS
DOCUMENT NUMBER: 122:150203
TITLE: Metal complexes with fluoro-containing macrocyclic ligands
INVENTOR(S): Platzek, Johannes; Raduechel, Bernd; Niedballa, Ulrich; Weinmann, Hans-Joachim; Bauer, Hans; Roth, Klaus
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4317588	A1	19941201	DE 1993-4317588	19930524
DE 4317588	C2	19980416		
WO 9427978	A1	19941208	WO 1994-EP1377	19940429
W: CA, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2163643	AA	19941208	CA 1994-2163643	19940429
EP 700393	A1	19960313	EP 1994-915566	19940429
EP 700393	B1	19971022		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08511248	T2	19961126	JP 1994-500148	19940429
AT 159522	E	19971115	AT 1994-915566	19940429
ES 2110753	T3	19980216	ES 1994-915566	19940429
NO 9504736	A	19951123	NO 1995-4736	19951123

US 5690909 A 19971125 US 1996-553432 19960319
PRIORITY APPLN. INFO.: DE 1993-4317588 19930524
WO 1994-EP1377 19940429

OTHER SOURCE(S): MARPAT 122:150203
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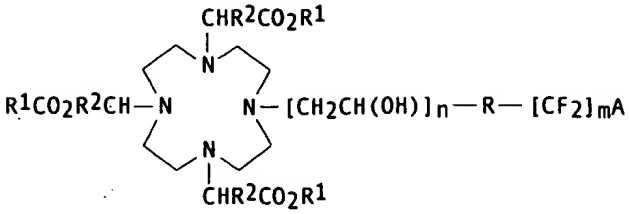

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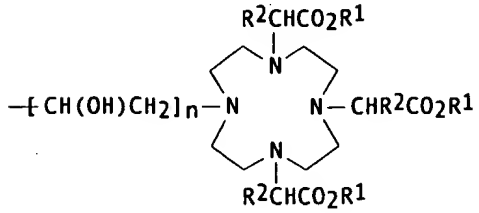
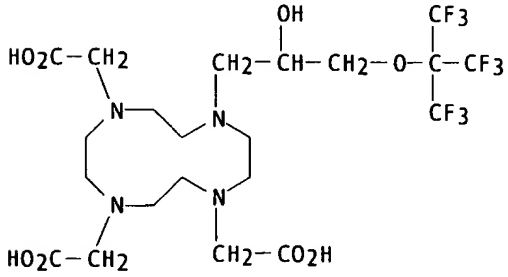


II

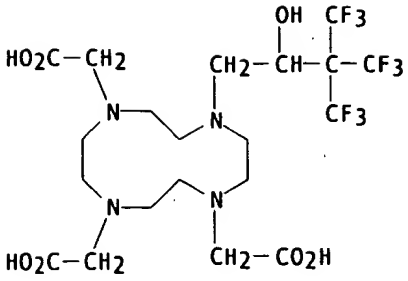
AB I (n = 0, 1; m = 0, 1; R1 = H or monovalent metal; R2 = H, straight-chained or branched alkyl, groups which can be substituted with 1-5 C1-C6-alkoxy, hydroxy-C1-C6-alkyl and/or OH groups; R = 1-3 CF3-group substituted straight-chained or branched C1-C10 alkyl group which can be substituted with 1-5 HO, C1-C6-alkoxy-C1-C6alkyl, OR3, CONR4R5, NR4R5 and/or NR4COR5 groups [R3 = straight-chained or branched C1-C4 alkyl groups and R4, R5 = R2; A = F for m = 1 and H or II for m = 0]) were prepd. Metal complexes of these macrocycles were prepd. for M = Sc-Cu; MO, Ru, La-Lu, Hf-Bi. Thus, I (R1 = R2 = H, R[CF2]mA = CF3) and its La, Pr, Dy, Eu complexes, I (R1 = R2 = H, R = [CH2CH(OH)]nR[CF2]mA = 2-hydroxy-2-trifluoromethylpropyl or 2-hydroxy-3-tert-nonafluorobutoxypropyl or 2-hydroxy-3,3,3-tris(trifluoromethyl)propyl) and their Dy, Eu, Pr complexes were prepd. These complexes may be used as agents in NMR imaging, x-ray diagnostics, temp. probes for detn. of the temp. of tissue by NMR.

IT **161228-18-8P 161228-19-9P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of)

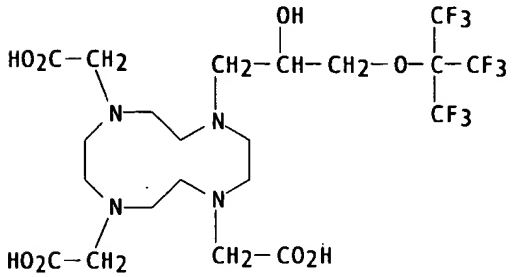
RN 161228-18-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[2,2,2-trifluoro-1,1-bis(trifluoromethyl)ethoxy]propyl]- (9CI) (CA INDEX NAME)



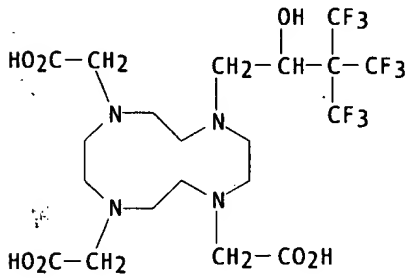
RN 161228-19-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[4,4,4-trifluoro-2-hydroxy-3,3-bis(trifluoromethyl)butyl]- (9CI) (CA INDEX NAME)



IT 161228-18-8DP, lanthanide complexes 161228-19-9DP, lanthanide complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 161228-18-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[2,2,2-trifluoro-1,1-bis(trifluoromethyl)ethoxy]propyl]- (9CI) (CA INDEX NAME)



RN 161228-19-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[4,4,4-trifluoro-2-hydroxy-3,3-bis(trifluoromethyl)butyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 61 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:358851 CAPLUS
DOCUMENT NUMBER: 122:299161
TITLE: Iodinated paramagnetic chelates and their use as contrast agents
INVENTOR(S): Uggeri, Fulvio; Anelli, Pier Lucio; Fedeli, Franco; Murru, Marcella; De Haen, Christoph
PATENT ASSIGNEE(S): Dibra S.p.A., Italy; Bracco S.p.A.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9427644	A1	19941208	WO 1994-EP1677	19940525
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9469965	A1	19941220	AU 1994-69965	19940525
EP 703790	A1	19960403	EP 1994-918782	19940525
EP 703790	B1	20000816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08510458	T2	19961105	JP 1994-500213	19940525
AT 195432	E	20000915	AT 1994-918782	19940525
ZA 9403816	A	19950131	ZA 1994-3816	19940601
US 5660814	A	19970826	US 1995-448476	19950530
PRIORITY APPLN. INFO.:			IT 1993-MI1155	19930602
			IT 1993-MI1274	19930615
			WO 1994-EP1677	19940525

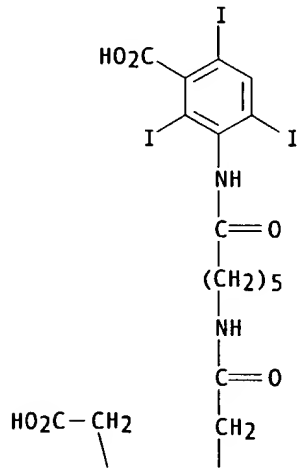
OTHER SOURCE(S): MARPAT 122:299161

AB The capacity of paramagnetic metal chelates to influence proton relaxation times during NMR imaging is enhanced by attaching to the chelating part of the mol. a polyiodinated component including at least a triiodinated arom. or heteroarom. x-ray opaque residue. Gadolinium complexes of some.

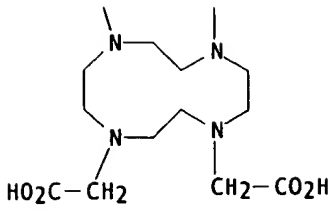
IT **160982-32-1DP**, gadolinium complexes **160982-33-2DP**, gadolinium complexes **160982-34-3DP**, gadolinium complexes
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of polyiodinated paramagnetic lanthanide chelates as NMR imaging contrast agents)

RN 160982-32-1 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[(3-carboxy-2,4,6-triiodophenyl)amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

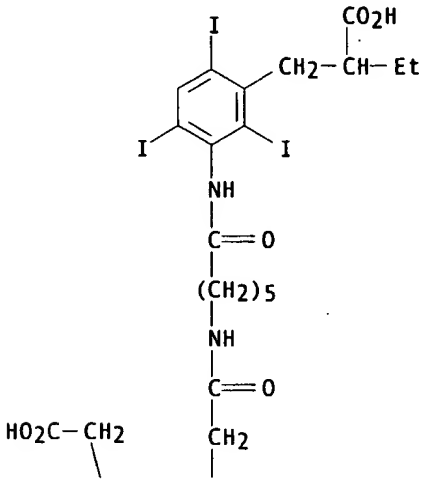


PAGE 2-A

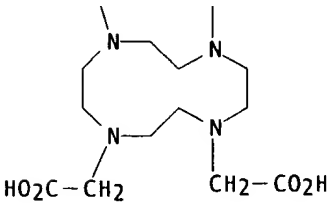


RN 160982-33-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[[3-(2-carboxybutyl)-2,4,6-triiodophenyl]amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

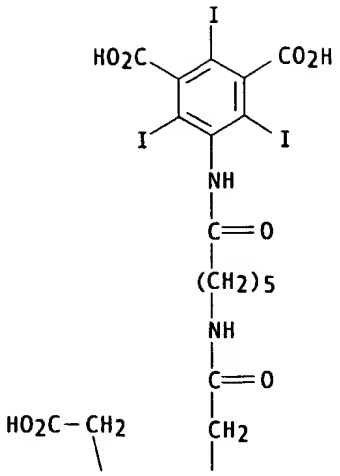
PAGE 1-A

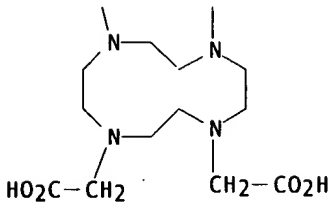


PAGE 2-A



RN 160982-34-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[6-[(3,5-dicarboxy-2,4,6-triiodophenyl)amino]-6-oxohexyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)





L10 ANSWER 62 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:305593 CAPLUS
DOCUMENT NUMBER: 122:75613
TITLE: Polychelants containing macrocyclic chelant moieties
INVENTOR(S): Sieving, Paul F.; Watson, Alan D.; Quay, Steven C.; Rocklage, Scott M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No.335,162, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5364613	A	19941115	US 1990-464865	19900116
CA 2051648	AA	19901008	CA 1990-2051648	19900405
WO 9012050	A1	19901018	WO 1990-EP565	19900405
W: AU, CA, FI, HU, JP, NO, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9054235	A1	19901105	AU 1990-54235	19900405
AU 656304	B2	19950202		
EP 474642	A1	19920318	EP 1990-906169	19900405
EP 474642	B1	19960626		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
EP 481526	A1	19920422	EP 1991-118887	19900405
EP 481526	B1	19970312		

R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE

JP 04504436	T2	19920806	JP 1990-505940	19900405
HU 60277	A2	19920828	HU 1990-3650	19900405
AT 139790	E	19960715	AT 1990-906169	19900405
ES 2088428	T3	19960816	ES 1990-906169	19900405
AT 150047	E	19970315	AT 1991-118887	19900405
ES 2098299	T3	19970501	ES 1991-118887	19900405
NO 9103920	A	19911127	NO 1991-3920	19911004
NO 178866	B	19960311		
NO 178866	C	19960619		
US 5554748	A	19960910	US 1993-175989	19931230
PRIORITY APPLN. INFO.:			US 1989-335162	19890407
			US 1990-464865	19900116
			WO 1990-EP565	19900405

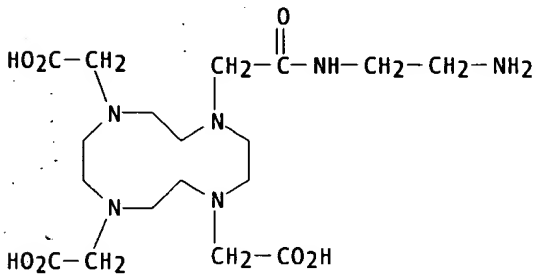
OTHER SOURCE(S): MARPAT 122:75613

AB Polychelants and their metal chelates are provided which are useful in diagnostic imaging and in radiotherapy and which coprise a plurality of macrocyclic chelant moieties, e.g, DOTA residues, conjugated to a polyamine backbone mol., e.g, polylysine. To produce a site-specific polychelate, one or more of the macrocyclic chelant carrying backbone mols. may be conjugated to a site-directed macromol., e.g. a protein. Thus, DOTA was reacted with iso-Bu chloroformate, and the resulting DOTA carboxycarbonic anhydride was reacted with poly-L-lysine to give polylysine-polyDOTA. The polylysine-polyDOTA was complexed with Gd and the Gd(polylysine-polyDOTA) was coupled to human serum albumin. An MRI formulation and biodistribution data are included.

IT **150467-20-2D**, reaction products with amine group-contg. backbone
160363-61-1D, reaction products with amine group-contg. backbone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polychelants contg. macrocyclic chelant moieties for use in radiotherapy and diagnostic imaging)

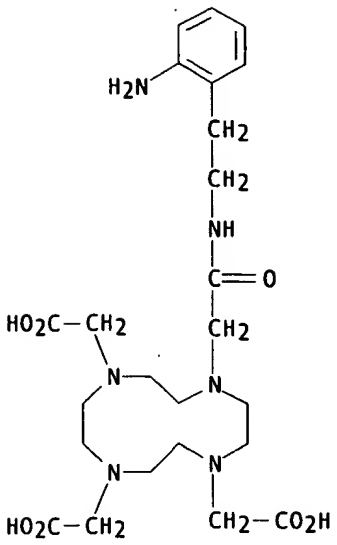
RN 150467-20-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

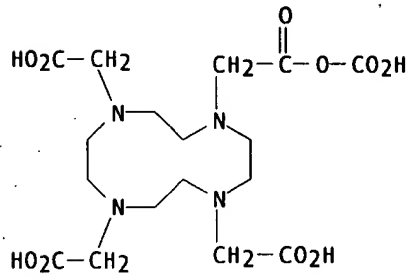


RN 160363-61-1 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-(2-aminophenyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



IT 160363-62-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(polychelants contg. macrocyclic chelant moieties for use in radiotherapy and diagnostic imaging, and their prepn.)
RN 160363-62-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, monoanhydride with carbonic acid (9CI) (CA INDEX NAME)



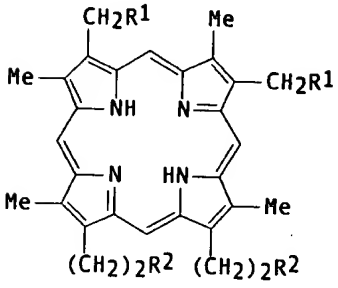
L10 ANSWER 63 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:649776 CAPLUS
DOCUMENT NUMBER: 121:249776
TITLE: Preparation of 3,8-disubstituted deuteroporphyrin derivatives and their metal complexes for diagnostic and therapeutic use
INVENTOR(S): Gries, Heinz; Hilger, Christoph Stephan; Maier, Franz Karl; Niedballa, Ulrich; Lee-Vaupel, Mary; Ebert, Wolfgang; Conrad, Juergen; Platzek, Johannes; Gaida, Josef
PATENT ASSIGNEE(S): Institut fuer Diagnostikforschung GmbH, Germany; Freien Universitaet Berlin
SOURCE: Ger. Offen., 49 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4232925	A1	19940331	DE 1992-4232925	19920928
WO 9407894	A1	19940414	WO 1993-EP2645	19930928

W: CA, JP, NO, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

ZA 9307194	A	19940421	ZA 1993-7194	19930928
EP 662972	A1	19950719	EP 1993-921875	19930928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08504399	T2	19960514	JP 1993-508701	19930928
NO 9501166	A	19950327	NO 1995-1166	19950327
US 5849259	A	19981215	US 1995-406881	19950524
PRIORITY APPLN. INFO.:			DE 1992-4232925	19920928
			WO 1993-EP2645	19930928

OTHER SOURCE(S): MARPAT 121:249776
GI



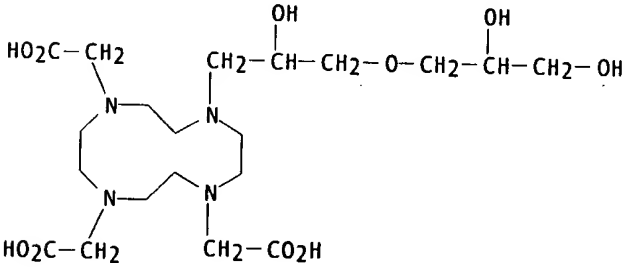
I

AB Metal complexes of porphyrins I [R1 = H, alkyl, aralkyl, OH, alkoxy; R2 = R3, CO2Z, (NH)oAqNHD; R3 = (C:M)(NR4)oAqNR5K; R4 = AqH; Z = alkyl, cation; A = C6H4O, C1-12 alkylene or C7-12 aralkylene interrupted with .gtoreq.1 O; D = H, COAY; Y = H, CO2Z; K = polycarboxylated complexing moiety; R5 = R4, D; o, q = 0, 1] are prepd. for use in NMR diagnosis, radiodiagnosis, and radiotherapy. Thus, N,N'-bis[9-carboxy-2,5,8-tris(carboxymethyl)-2,5,8-triazanonylcarbamoyl]mesoporphyrin IX 13,17-diamide di-Gd complex di-Na salt (II), administered i.v. to colon carcinoma-bearing mice, selectively enhanced the signal from the liver and kidneys in nuclear spin tomog. over that from muscle and tumor tissues. II was prepd. by reaction of mesoporphyrin IX 13,17-dihydrazide with DTPA mono-Et ester monoanhydride, followed by complexation with Gd and sapon. with NaOH.

IT 143228-97-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation with gadolinium)

RN 143228-97-1 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-(2,3-dihydroxypropoxy)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 64 OF 83 CAPLUS COPYRIGHT 2001 ACS

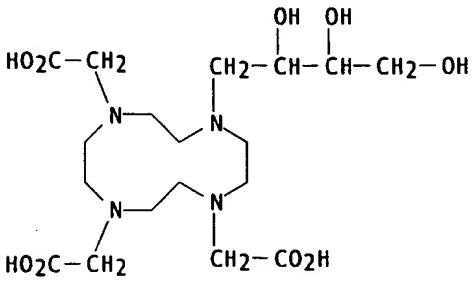
ACCESSION NUMBER: 1994:457541 CAPLUS

DOCUMENT NUMBER: 121:57541

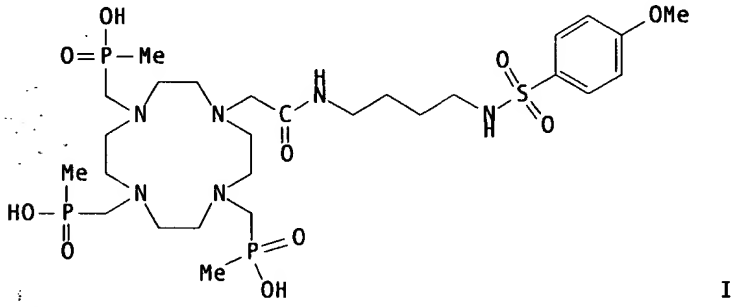
TITLE: Preparation of N-hydroxyalkyl-N',N'',N'''-tris(carboxylalkyl)-1,4,7,10-tetraazacyclododecane- and -1,4,8,11-tetraazacyclotetradecane derivatives and their metal complexes.

INVENTOR(S): Tilstam, Ulf; Boerner, Helmut; Nickisch, Klaus; Gries,

(prepn. of)
RN 138147-53-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3,4-trihydroxybutyl)- (9CI) (CA INDEX NAME)

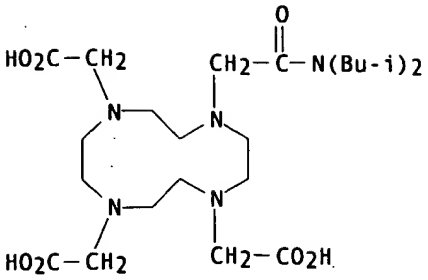


L10 ANSWER 65 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:435685 CAPLUS
DOCUMENT NUMBER: 121:35685
TITLE: Synthesis of charged and uncharged complexes of gadolinium and yttrium with cyclic polyazaphosphinic acid ligands for in vivo applications
AUTHOR(S): Pulukkody, Kanthi P.; Norman, Timothy J.; Parker, David; Royle, Louise; Broan, Christopher J.
CORPORATE SOURCE: Dep. Chem., Univ. Durham, Durham, DH1 3LE, UK
SOURCE: J. Chem. Soc., Perkin Trans. 2 (1993), (4), 605-20
CODEN: JCPKBH; ISSN: 0300-9580
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:35685
GI

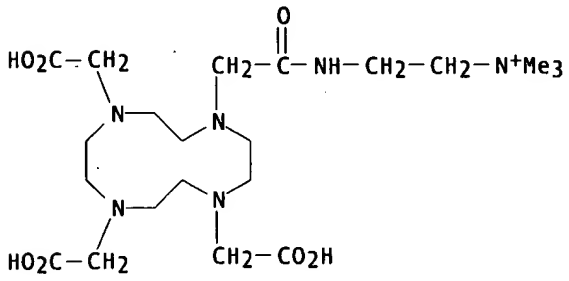


I

AB The synthesis of 18 new macrocyclic complexing agents incorporating phosphinic acid (and carboxylic acid) groups, e.g., I, is reported, based on the 1,4,7,10-tetraazacyclododecane ring. Through selective functionalization of one ring nitrogen or by changing the nature of the P-substituent, anion, neutral and cationic complexes of yttrium and gadolinium may be prepd. of varying lipophilicity. Diamagnetic complexes have been characterized by 1H, 31P and 89Y NMR spectroscopy, and the rate of uptake of 90Y of selected ligands compared. The kinetics of dissocn. of nine gadolinium complexes has been measured in the pH range 1-2 using 153Gd-labeled complexes. Charge-neutral complexes dissoc. more slowly than their anionic analogs, and the phosphinate complexes, although slightly less stable than their carboxylate analogs, are nevertheless sufficiently kinetically inert for in vivo applications.
IT 148932-58-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with yttrium oxide)
RN 148932-58-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[bis(2-methylpropyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

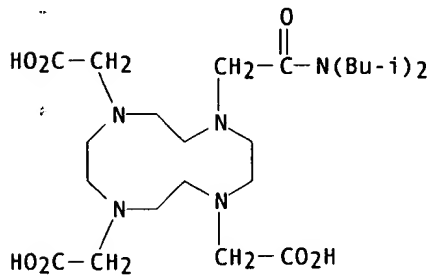


IT **148910-49-0P 148910-50-3P 148910-54-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 148910-49-0 CAPLUS
CN Ethanaminium, N,N,N-trimethyl-2-[[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]amino]-, chloride (9CI) (CA INDEX NAME)



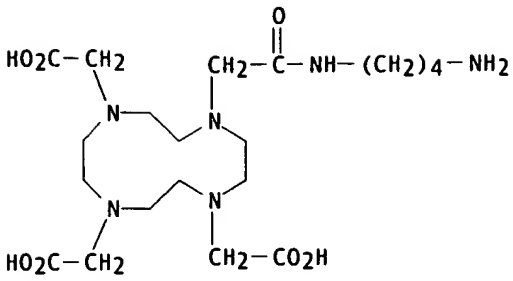
● Cl⁻

RN 148910-50-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[bis(2-methylpropyl)amino]-2-oxoethyl]-, trihydrobromide (9CI) (CA INDEX NAME)



●3 HBr

RN 148910-54-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(4-aminobutyl)amino]-2-oxoethyl]-, trihydrobromide (9CI) (CA INDEX NAME)



●3 HBr

L10 ANSWER 66 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:200413 CAPLUS
DOCUMENT NUMBER: 120:200413
TITLE: Labeling Monoclonal Antibodies with 90Yttrium- and 111Indium-DOTA Chelates: A Simple and Efficient Method
AUTHOR(S): Li, Min; Meares, Claude F.; Zhong, Gao-Ren; Miers, Laird; Xiong, Cheng-Yi; DeNardo, Sally J.
CORPORATE SOURCE: Department of Chemistry, University of California, Davis, CA, 95616, USA
SOURCE: Bioconjugate Chem. (1994), 5(2), 101-4
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English

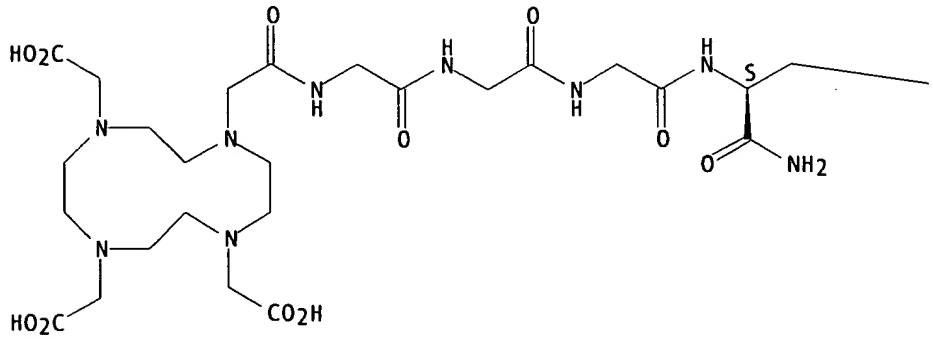
AB Yttrium-90 and indium-111 have been attached to a monoclonal antibody with a bifunctional chelating agent (DOTA-peptide). Using the unique features of this DOTA-peptide and its complexes with trivalent yttrium and indium, the bifunctional chelating agent was prelabeled with either radiometal and then conjugated to chimeric monoclonal antibody L6. Both radiolabeling procedures and yield are suitable for the practical prepn. of radiopharmaceuticals. Biodistribution studies in tumor-bearing mice showed that, e.g., on day 3 after i.v. injection of a 90Y immunoconjugate, liver uptake was 5.4 .+-. 1.5% ID/g, bone uptake 2.0 .+-. 0.5% ID/g, and tumor uptake 18.0 .+-. 8.0% ID/g.

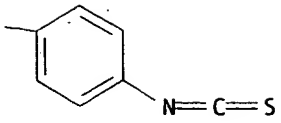
IT 149206-88-2
RL: USES (Uses)
(complexation of, with indium-111 and yttrium-90)

RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

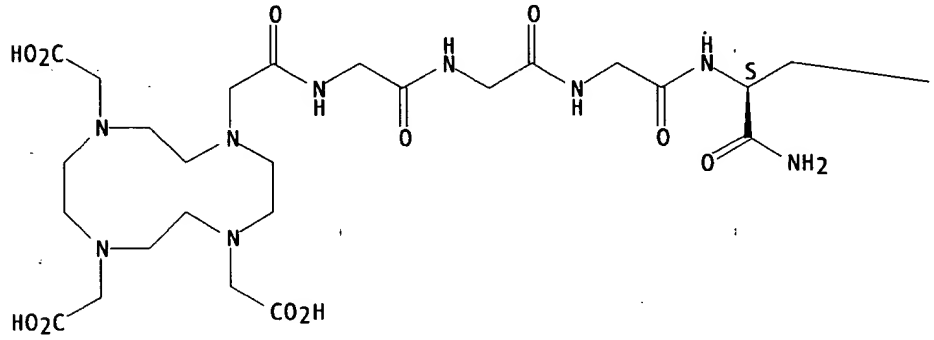




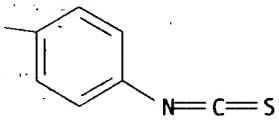
IT **149206-88-2DP**, complexes with indium-111 and yttrium-90, conjugates with monoclonal antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biodistribution of, as radiopharmaceuticals)
RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L10 ANSWER 67 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:685183 CAPLUS
DOCUMENT NUMBER: 119:285183
TITLE: Aminocarboxylate ligands having substituted aromatic amide moieties
INVENTOR(S): Pillai, Radhakrishna; Marinelli, Edmund R.; Ranganathan, Ramachandran S.; Tweedle, Michael F.; Kang, Sang Ihn
PATENT ASSIGNEE(S): USA
SOURCE: Can. Pat. Appl., 71 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

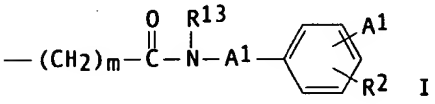
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2074867	AA	19930202	CA 1992-2074867	19920729
ZA 9205521	A	19930428	ZA 1992-5521	19920722

AU 9220615	A1	19930204	AU 1992-20615	19920729
NO 9203038	A	19930202	NO 1992-3038	19920731
HU 62906	A2	19930628	HU 1992-2513	19920731
JP 05208920	A2	19930820	JP 1992-205097	19920731
JP 2538165	B2	19960925		
CN 1069027	A	19930217	CN 1992-109214	19920801
EP 543482	A1	19930526	EP 1992-307091	19920803

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1991-738998 19910801

GI



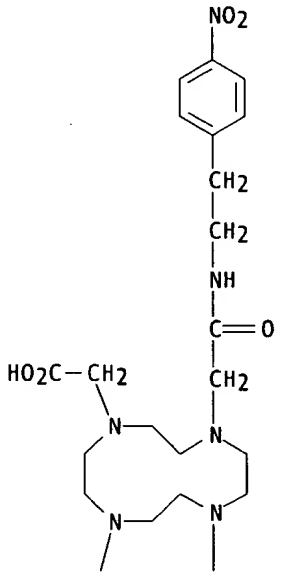
I

AB A diagnostic agent comprises aminocarboxylate ligand complexed with paramagnetic metal ion wherein a N atom within said aminocarboxylate is substituted with a substituted arom. amide group. The substituted arom. amide group is of the formula I, wherein A1 is -(CH2)m' and (CH2)m' may independently be substituted with alkyl or hydroxyalkyl; R1 and R2 are each independently hydrogen, alkyl, NCS, -(CO)-NR3R4, NR3COR9, where R9 is alkyl or hydroxyalkyl, with the proviso that at least one of R1 and R2 must be other than hydrogen; R3 and R4 are independently hydrogen, alkyl, arylalkyl, aryl, alkoxy, and hydroxyalkyl; R12 is hydrogen, alkyl, or hydroxyalkyl; R13 is hydrogen, alkyl aryl, or alkoxy; m and m' are independently 1 to 5; and multimeric forms thereof. Application for x-ray contrast agents, imaging radio pharmaceuticals, therapeutic radiopharmaceutically and magnetic resonance imaging relaxation agents is indicated.

IT **150583-69-0**
RL: RCT (Reactant)
(diagnostic agent contg.)

RN 150583-69-0 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-(4-nitrophenyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



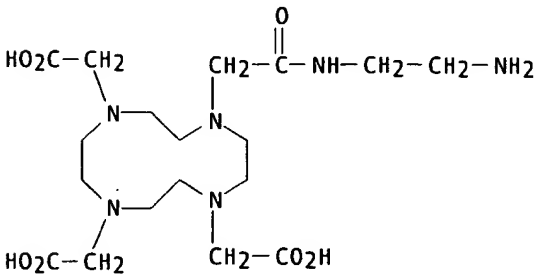
L10 ANSWER 68 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:620702 CAPLUS
DOCUMENT NUMBER: 119:220702
TITLE: Dendrimeric polychelants as imaging agents
INVENTOR(S): Watson, Alan D.
PATENT ASSIGNEE(S): Cockbain, Jilian Roderick Michaelson, UK; Nycomed Salutar, Inc.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

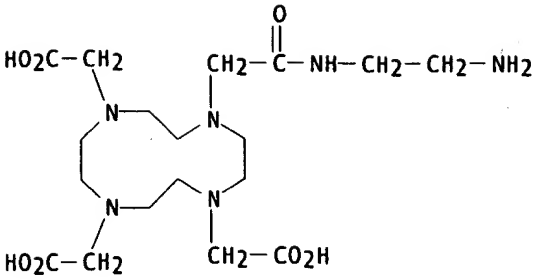
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306868	A1	19930415	WO 1992-EP2308	19921006
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9226757	A1	19930503	AU 1992-26757	19921006
AU 671601	B2	19960905		
EP 607222	A1	19940727	EP 1992-920822	19921006
EP 607222	B1	19981223		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 07503031	T2	19950330	JP 1992-506624	19921006
AT 174800	E	19990115	AT 1992-920822	19921006
PRIORITY APPLN. INFO.:			US 1991-772349	19911007
			WO 1992-EP2308	19921006

AB Polyvalent chelating agents, comprising multiple macrocyclic chelating moieties conjugated to a .ltoreq.5th-generation dendrimer backbone, and their metal chelates are useful in diagnostic imaging and radiotherapy. To produce a site-specific agent, .gtoreq.1 of the chelating agent-carrying backbone mols. may be conjugated to a site-directed mol., e.g. a protein. Thus, Me acrylate reacted with NH3-MeOH to form N(CH2CH2CO2Me)3, which combined with H2NCH2CH2NH2 to form a 1st-generation polyaminoamido starburst dendrimer; further generations were produced by alternate reaction of the product with Me acrylate and H2NCH2CH2NH2. A 2nd-generation dendrimer was coupled to 12 equiv. of DOTA carboxycarbonic anhydride, complexed with Gd, and conjugated via succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate to 2-iminothiolane-activated antibody L6.

IT 150467-20-2D, conjugates with starburst dendritic polymers, metal complexes 151790-71-5D, conjugates with starburst dendritic polymers, metal complexes
RL: BIOL (Biological study)
(for diagnostic imaging and radiotherapy)

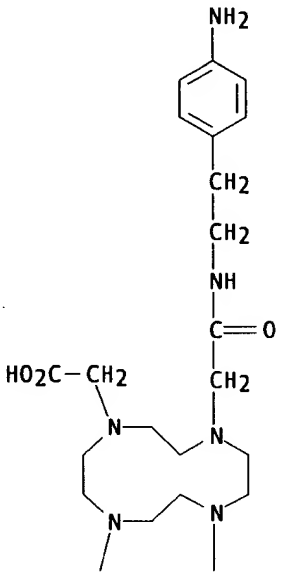
RN 150467-20-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-aminoethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)





RN 151790-71-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[[2-(4-aminophenyl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L10 ANSWER 69 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:490207 CAPLUS
DOCUMENT NUMBER: 119:90207
TITLE: Synthesis, metal chelate stability studies, and enzyme digestion of a peptide-linked DOTA derivative and its corresponding radiolabeled immunoconjugates
AUTHOR(S): Li, Min; Meares, Claude F.
CORPORATE SOURCE: Dep. Chem., Univ. California, Davis, CA, 95616-0935, USA
SOURCE: Bioconjugate Chem. (1993), 4(4), 275-83
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By directly coupling a tetrapeptide to DOTA through an amide bond, a novel DOTA deriv., DOTA-glycylglycylglycyl-L-p-nitrophenylalanine amide, was synthesized. This new precursor bifunctional chelating agent was converted to DOTA-glycylglycylglycyl-L-p-isothiocyanatophenylalanine and conjugated to monoclonal antibody Lym-1. Serum stability studies show

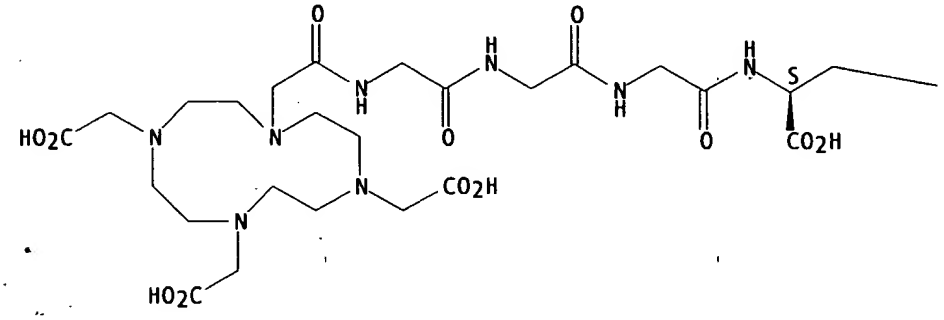
that the radiolabeled conjugates are kinetically inert under physiol. conditions. The rates of loss of radiometals in human serum are 0.1% per day for In3+, 0.02% per day for Y3, and 0.3% per day for Cu2+-labeled immunoconjugates. In the presence of the liver enzyme cathepsin B, an in vitro digestion of 114mIn-labeled conjugate yields a small fragment contg. 114mIn. Characterization of the cleavage products shows that this liver enzyme hydrolyzes the peptide linkage before the phenylalanine residue, freeing the In-DOTA-triglycine complex from the conjugate. However, the liver enzyme cathepsin D does not cleave the linkage over the span of 7 days.

IT **149206-87-1P 149206-88-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and coupling to monoclonal antibody)

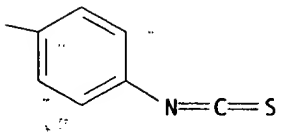
RN 149206-87-1 CAPLUS
CN L-Phenylalanine, 4-isothiocyanato-N-[N-[N-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycyl]glycyl]glycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



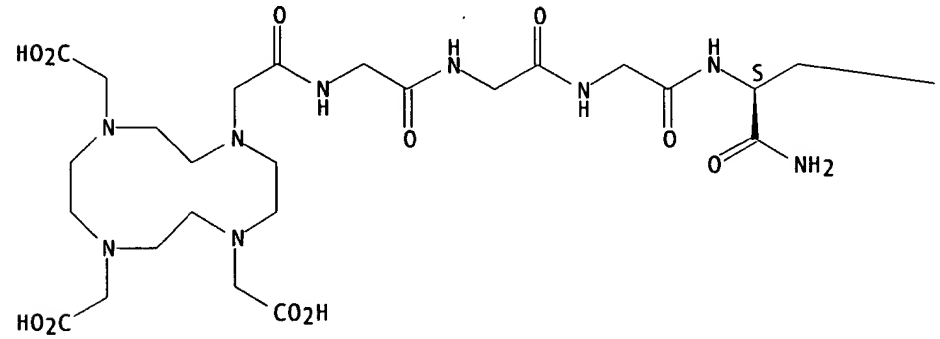
PAGE 1-B



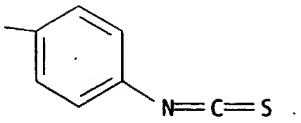
RN 149206-88-2 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-isothiocyanato- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



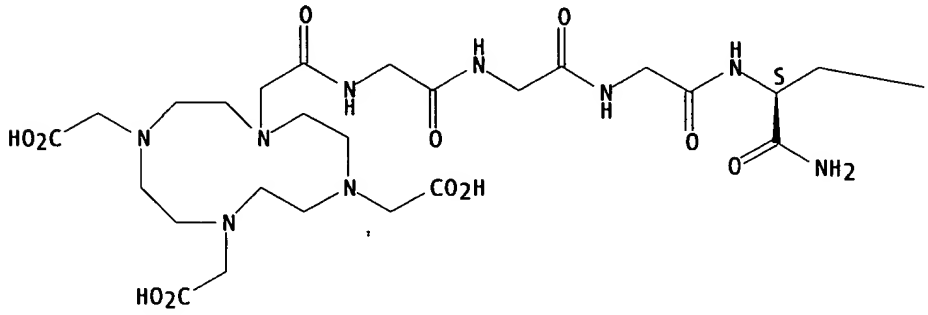
PAGE 1-B



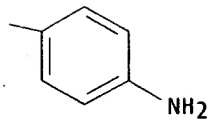
IT 149226-85-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and isothiocyanatylation of)
RN 149226-85-7 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecyl]acetyl]glycylglycylglycyl-4-amino- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



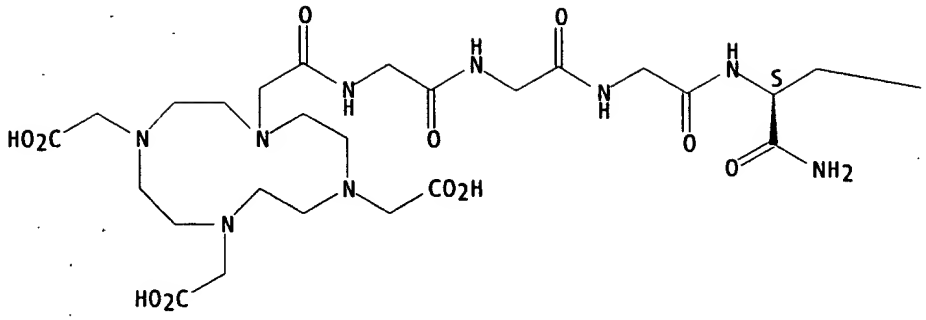
PAGE 1-B



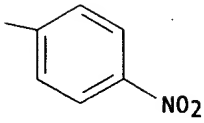
IT' 149206-86-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
RN 149206-86-0 CAPLUS
CN L-Phenylalaninamide, N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycylglycylglycyl-4-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



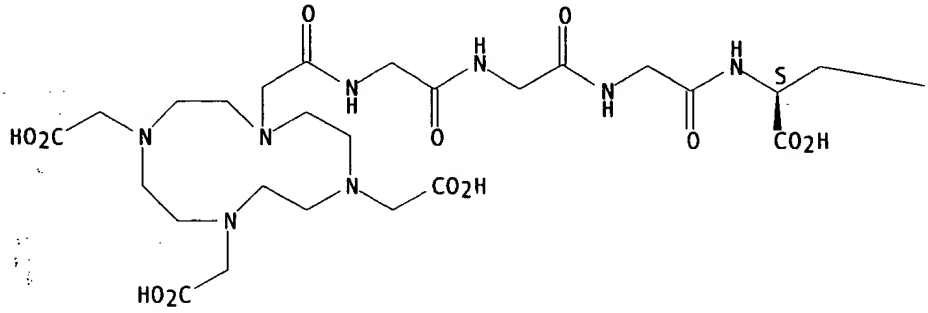
PAGE 1-B



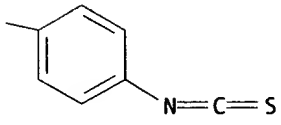
IT 149206-87-1DP, radiometal-monoclonal antibody conjugates
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and stability and enzyme digestion of)
RN 149206-87-1 CAPLUS
CN L-Phenylalanine, 4-isothiocyanato-N-[N-[N-[N-[[4,7,10-tris(carboxymethyl)-1,4,7,10-tetraazacyclododec-1-yl]acetyl]glycyl]glycyl]glycyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L10 ANSWER 70 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:109826 CAPLUS
DOCUMENT NUMBER: 118:109826
TITLE: Preparation of macrocyclic complexes and gadolinium for NMR imaging and radiographic diagnostics
INVENTOR(S): Schmitt-Willich, Heribert; Platzek, Johannes; Gries,

Heinz; Schuhmann-Giampieri, Gabriele; Frenzel, Thomas
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

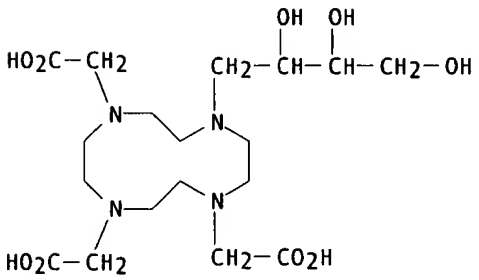
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 512661	A1	19921111	EP 1992-250110	19920507
EP 512661	B1	19980114		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
DE 4115789	A1	19921112	DE 1991-4115789	19910510
JP 05214096	A2	19930824	JP 1992-114636	19920507
AT 162082	E	19980115	AT 1992-250110	19920507
ES 2113918	T3	19980516	ES 1992-250110	19920507
CA 2068266	AA	19921111	CA 1992-2068266	19920508
NO 9201832	A	19921111	NO 1992-1832	19920508
AU 9216139	A1	19921112	AU 1992-16139	19920508
AU 661305	B2	19950720		
IL 101817	A1	19980310	IL 1992-101817	19920510
ZA 9203394	A	19930127	ZA 1992-3394	19920511
US 5876698	A	19990302	US 1992-881269	19920511

PRIORITY APPLN. INFO.: DE 1991-4115789 19910510

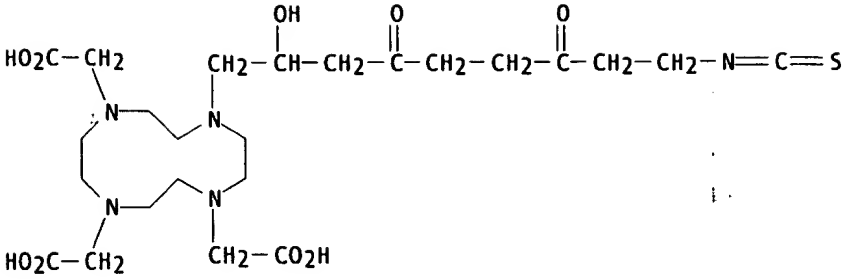
AB Polylysine complexes with macrocyclic complexes such as Gd-triscarboxymethyltetraazacyclododecane derivs. are prepd. and their magnetic relaxation properties are studied for use in MRI and radiog. diagnostics. Thus, 1,4,7-triscarboxymethyl-1,4,7,10-tetraazacyclododecane was treated with 2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethylene oxide in dioxane to give the tetraazacyclododecane deriv. followed by complexation with Gd oxide. This was then allowed to react with NaIO4 followed by treatment with poly(L-lysine)-HCl and subsequent redn. with NaCNBH3. The T1 relaxivity of the complex was shown to be 12.33 and 12.75 L/mmol.sec in water and plasma, resp.

IT **138147-53-2DP**, gadolinium complexes, reaction products with polylysine **146271-04-7DP**, gadolinium complexes, reaction products with polylysine **146271-05-8DP**, gadolinium complexes, reaction products with polylysine, derivs. **146271-09-2DP**, gadolinium complexes, reaction products with polylysine
RL: PREP (Preparation)
(prepn. and NMR relaxation parameters of, radiog. diagnostics and MRI in relation to)

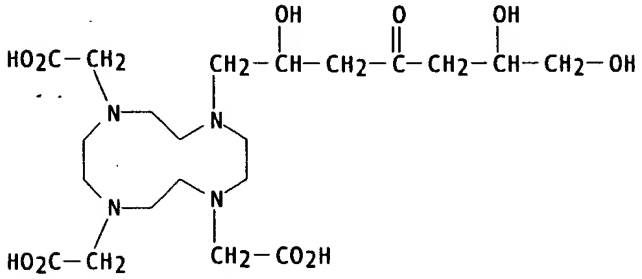
RN 138147-53-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3,4-trihydroxybutyl)- (9CI) (CA INDEX NAME)



RN 146271-04-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-9-isothiocyanato-4,7-dioxononyl)- (9CI) (CA INDEX NAME)



RN 146271-05-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,6,7-trihydroxy-4-oxoheptyl)- (9CI) (CA INDEX NAME)



RN 146271-09-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-(2-ethoxy-1-methyl-2-oxoethyl)phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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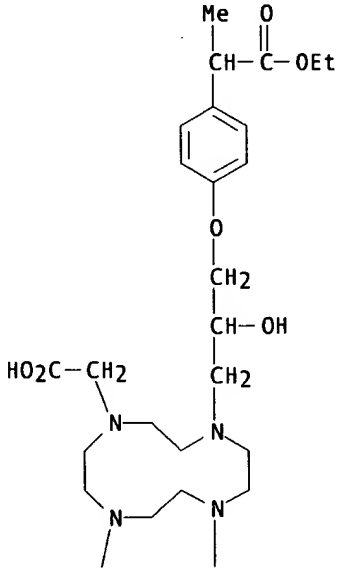


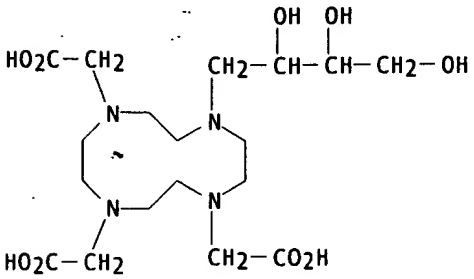
PAGE 2-A

IT 138147-53-2P 146271-09-2P
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. and complexation of, with gadolinium oxide)

RN 138147-53-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3,4-trihydroxybutyl)- (9CI) (CA INDEX NAME)



RN 146271-09-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-(2-ethoxy-1-methyl-2-oxoethyl)phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

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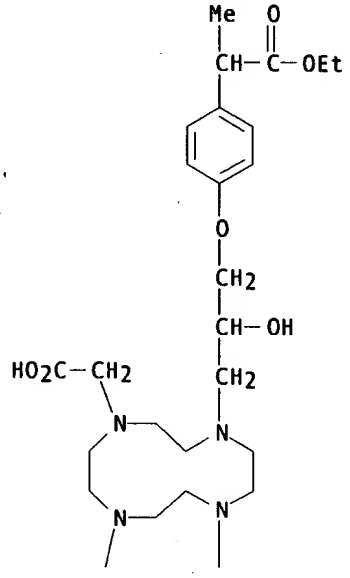


PAGE 2-A

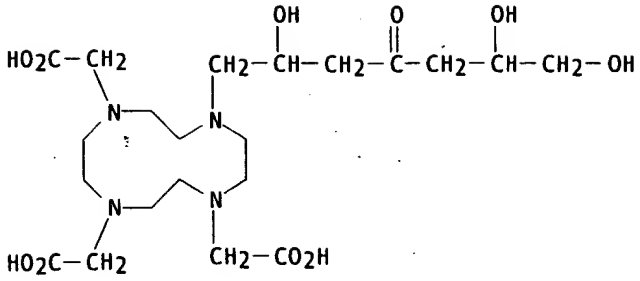
IT 146271-05-8P

RL: PREP (Preparation)

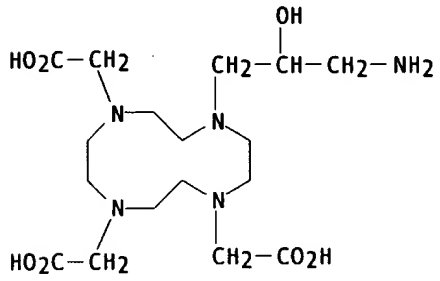
(prepn. and complexation with gadolinium oxide)

RN 146271-05-8 CAPLUS

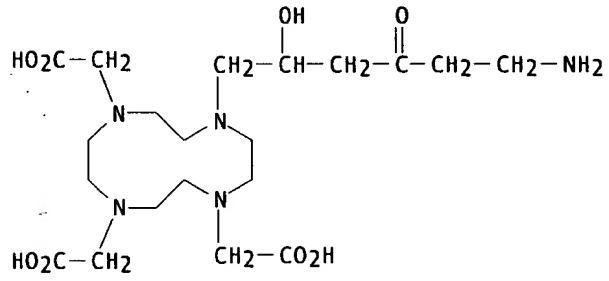
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,6,7-trihydroxy-4-oxoheptyl)- (9CI) (CA INDEX NAME)



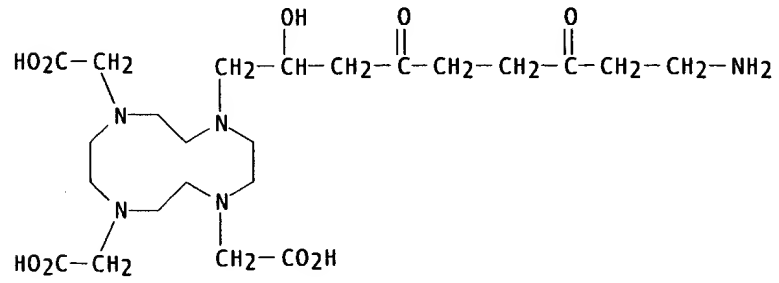
IT **146270-94-2DP**, gadolinium complexes **146270-98-6DP**, gadolinium complexes **146271-03-6DP**, gadolinium complexes
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with thiophosgene)
RN 146270-94-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(3-amino-2-hydroxypropyl)- (9CI) (CA INDEX NAME)



RN 146270-98-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(6-amino-2-hydroxy-4-oxohexyl)- (9CI) (CA INDEX NAME)

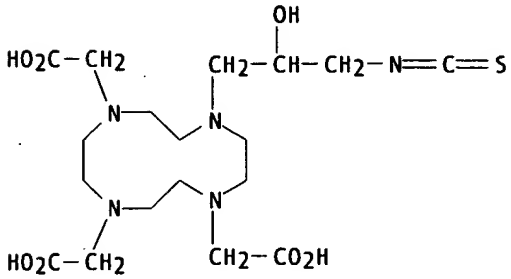


RN 146271-03-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(9-amino-2-hydroxy-4,7-dioxononyl)- (9CI) (CA INDEX NAME)

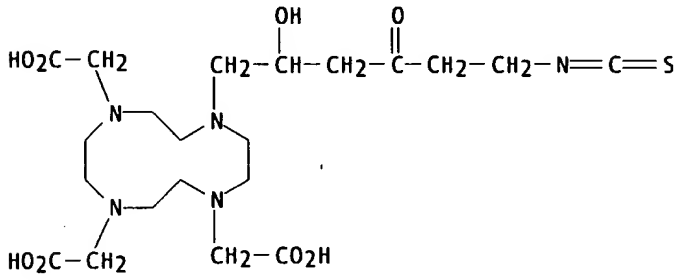


IT **146270-95-3DP**, gadolinium complexes, reaction products with polylysine **146270-99-7DP**, gadolinium complexes, reaction

products with polylysine
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 146270-95-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-3-isothiocyanatopropyl)- (9CI) (CA INDEX NAME)



RN 146270-99-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-6-isothiocyanato-4-oxohexyl)- (9CI) (CA INDEX NAME)

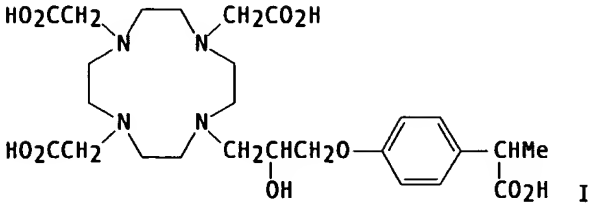


L10 ANSWER 71 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:551027 CAPLUS
DOCUMENT NUMBER: 117:151027
TITLE: 1,4,7,10-tetraazacyclododecane derivatives [e.g. 10-[2-hydroxy-3-[4-[2-(carboxyethyl)phenoxy]propyl-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane], process for their preparation and contrast agents for NMR tomography containing them
INVENTOR(S): Platzek, Johannes; Gries, Heinz; Weinmann, Hans Joachim; Press, Wolf Ruediger; Vogler, Hubert
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 485045	A2	19920513	EP 1991-250305	19911107
EP 485045	A3	19921028		
EP 485045	B1	19981230		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4035760	A1	19920514	DE 1990-4035760	19901108
CA 2055093	AA	19920509	CA 1991-2055093	19911107
NO 9104356	A	19920511	NO 1991-4356	19911107
JP 04288063	A2	19921013	JP 1991-318548	19911107
AT 175201	E	19990115	AT 1991-250305	19911107
ES 2128307	T3	19990516	ES 1991-250305	19911107
FI 9105282	A	19920509	FI 1991-5282	19911108

AU 9187726	A1	19920514	AU 1991-87726	19911108
ZA 9108893	A	19920826	ZA 1991-8893	19911108
US 5277895	A	19940111	US 1991-789178	19911108
US 5871709	A	19990216	US 1994-179552	19940110
PRIORITY APPLN. INFO.:			DE 1990-4035760	19901108
			US 1991-789178	19911108

OTHER SOURCE(S): MARPAT 117:151027
GI



I

AB Certain metal ion complexes of 1,4,7,10-tetraazocyclododecane derivs. are claimed. A process for their prepn. and pharmaceuticals contg. them are claimed. The compds. thus claimed are contrast agents for NMR tomog. Ring opening of 2,3-epoxy-1-[4-[2-(ethoxycarbonyl)ethyl]phenoxy]propane with 1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane gave 10-[2-hydroxy-3-[4-(2-carboxyethyl)phenoxy]propyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane (I). A parenteral soln. contained I-gadolinium complex, Trometamine and water. The relaxivity of I-gadolinium complex in human plasma at 38.degree. was 7.28 mMs-1.

IT **143228-92-6P 143228-93-7P 143228-96-0P**
143229-03-2P 143229-04-3P 143229-05-4P
143229-06-5P 143229-07-6P 143229-08-7P
143229-09-8P 143229-10-1P 143229-11-2P
143229-12-3P 143229-13-4P 143244-99-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of, with gadolinium)

RN 143228-92-6 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[oxy(2-hydroxy-3,1-propanediyl)]]bis- (9CI) (CA INDEX NAME)

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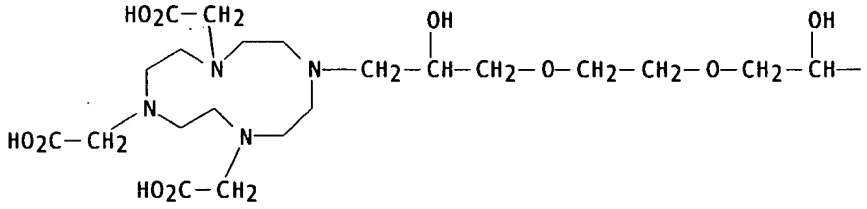
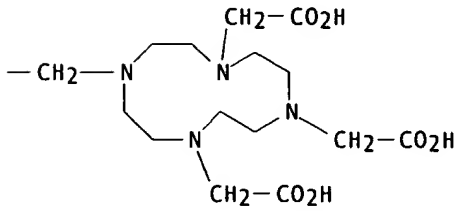


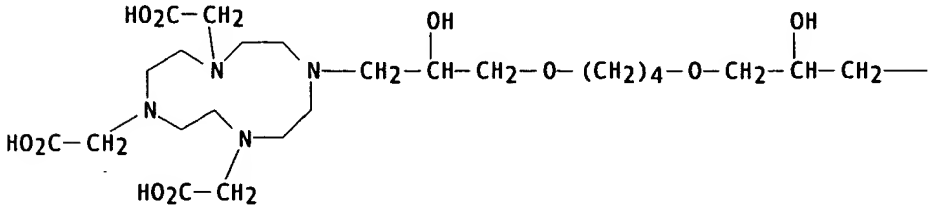
PAGE 1-B



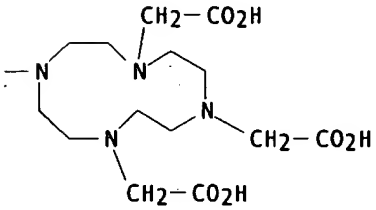
RN 143228-93-7 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,4-butanediylbis[oxy(2-hydroxy-3,1-propanediyl)]]bis- (9CI) (CA INDEX NAME)

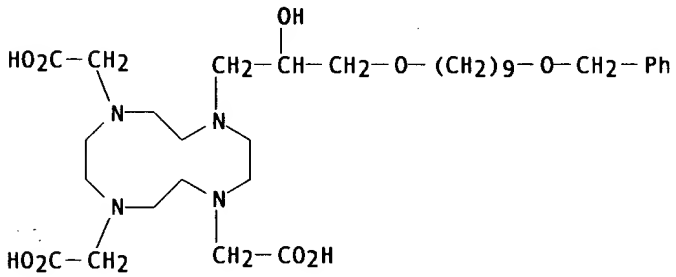
PAGE 1-A



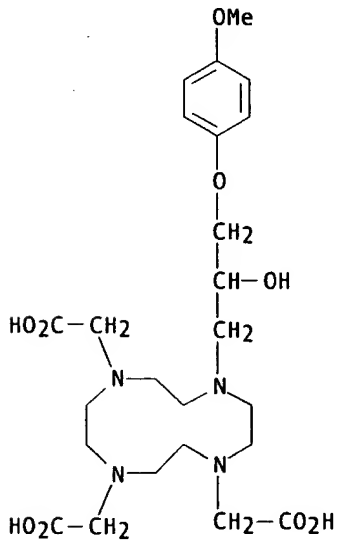
PAGE 1-B

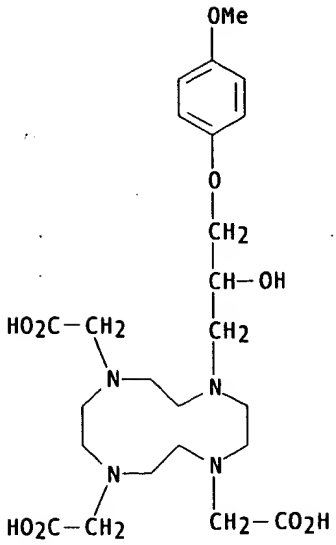


RN 143228-96-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[[9-(phenylmethoxy)nonyl]oxy]propyl]- (9CI) (CA INDEX NAME)



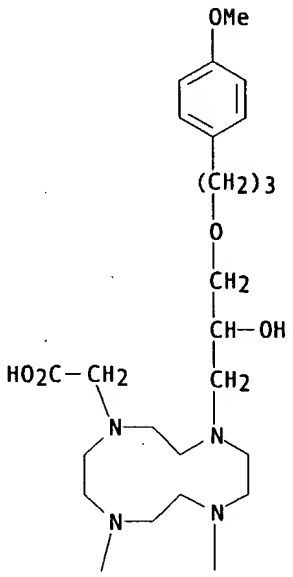
RN 143229-03-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-(4-methoxyphenoxy)propyl]- (9CI) (CA INDEX NAME)





RN 143229-04-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[3-(4-methoxyphenyl)propoxy]propyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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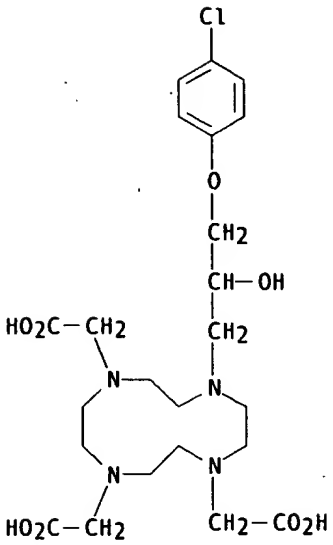
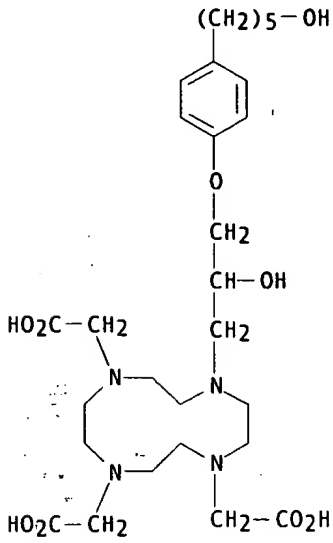
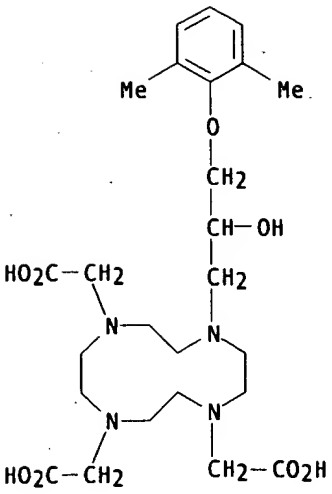
RN 143229-05-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-(4-chlorophenoxy)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



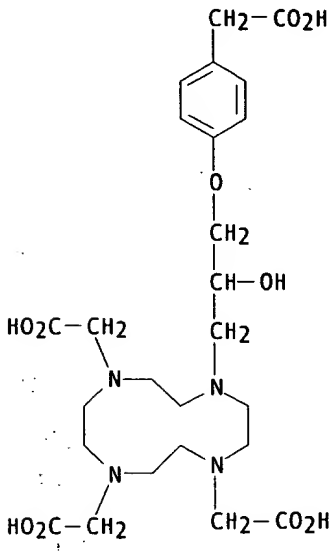
RN 143229-06-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[4-(5-hydroxypentyl)phenoxy]propyl]- (9CI) (CA INDEX NAME)



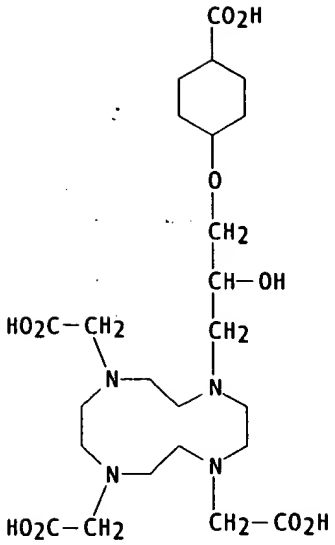
RN 143229-07-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-(2,6-dimethylphenoxy)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



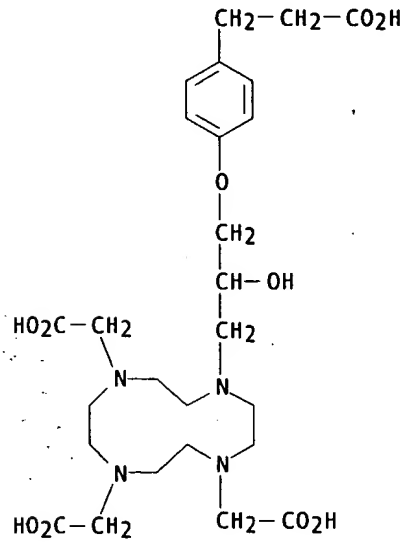
RN 143229-08-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-(carboxymethyl)phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



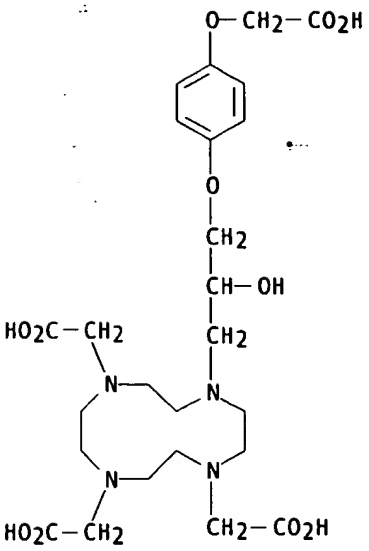
RN 143229-09-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[(4-carboxycyclohexyl)oxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



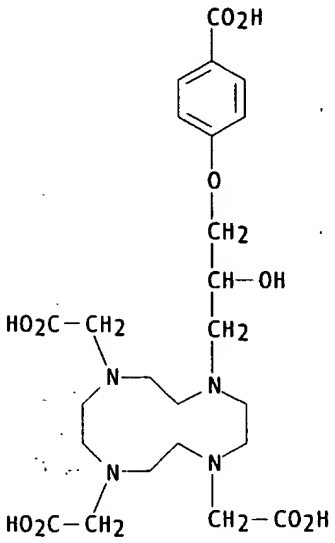
RN 143229-10-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-(2-carboxyethyl)phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



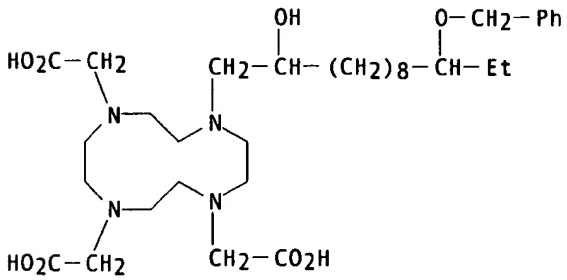
RN 143229-11-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[4-(carboxymethoxy)phenoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 143229-12-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-(4-carboxyphenoxy)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



RN 143229-13-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-11-(phenylmethoxy)tridecyl]- (9CI) (CA INDEX NAME)



RN 143244-99-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[oxybis(2-hydroxy-3,1-propanediyl)]bis- (9CI) (CA INDEX NAME)

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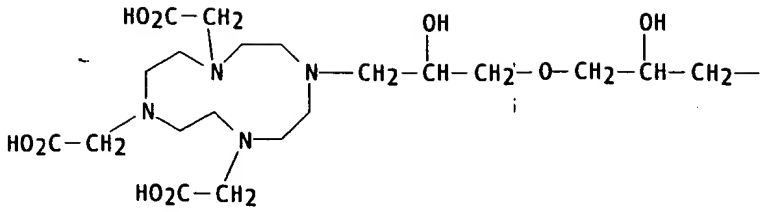

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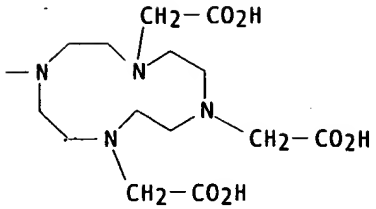
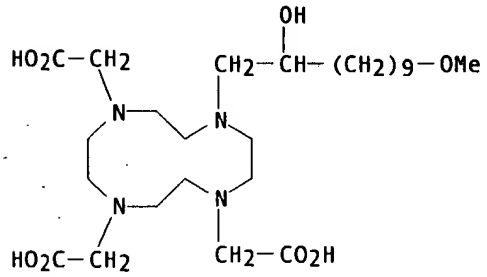
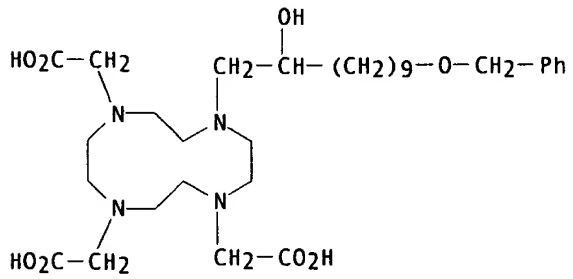


IT 143228-95-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of, with gadolinium or dysprosium)
RN 143228-95-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-11-methoxyundecyl)- (9CI) (CA INDEX NAME)

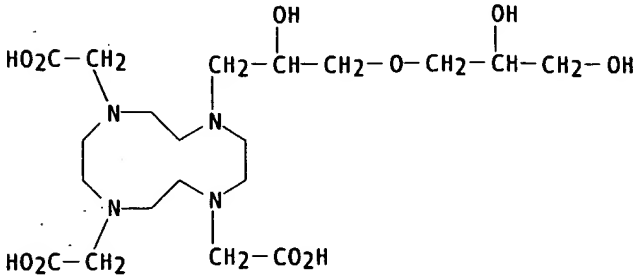


IT 143228-94-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of, with gadolinium or iron or manganese)
RN 143228-94-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-11-(phenylmethoxy)undecyl]- (9CI) (CA INDEX NAME)

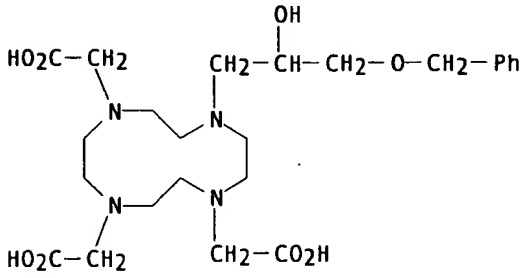


IT 143228-97-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of, with gadolinium, europium, dysprosium or ytterbium)

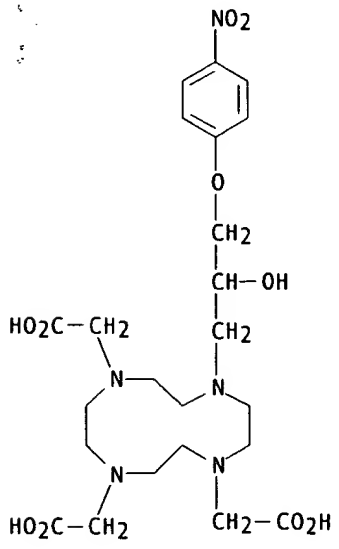
RN 143228-97-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-(2,3-dihydroxypropoxy)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



IT 143229-00-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of, with gadolinium, europium, or ytterbium)
RN 143229-00-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-(phenylmethoxy)propyl]- (9CI) (CA INDEX NAME)

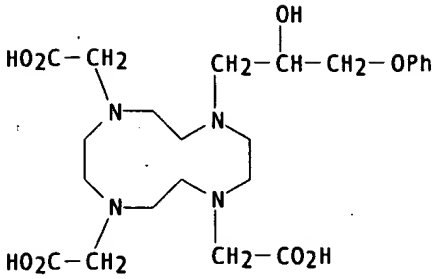


IT 143229-01-0P 143229-02-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. and complexation of, with gadolinium)
RN 143229-01-0 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-(4-nitrophenoxy)propyl]- (9CI) (CA INDEX NAME)

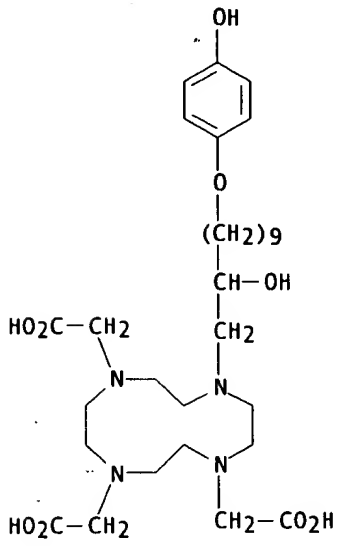


RN 143229-02-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-3-

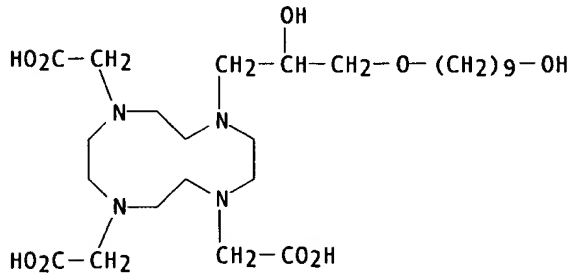
phenoxypropyl)- (9CI) (CA INDEX NAME)



IT 143229-15-6P 143229-18-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 143229-15-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-11-(4-hydroxyphenoxy)undecyl]- (9CI) (CA INDEX NAME)



RN 143229-18-9 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-hydroxy-3-[(9-hydroxynonyl)oxy]propyl]- (9CI) (CA INDEX NAME)



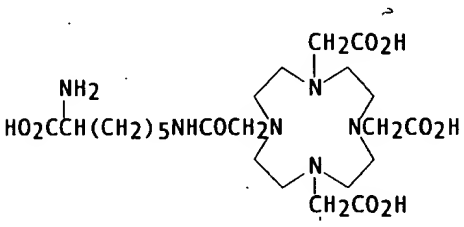
L10 ANSWER 72 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:485989 CAPLUS
DOCUMENT NUMBER: 117:85989
TITLE: Novel magnetic resonance imaging agents
INVENTOR(S): Rajagopalan, Raghavan; Vanderipe, Donald R.
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9204919	A1	19920402	WO 1991-US6531	19910910
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5162109	A	19921110	US 1990-581861	19900913
CA 2068424	AA	19920314	CA 1991-2068424	19910910
AU 9188515	A1	19920415	AU 1991-88515	19910910
EP 500919	A1	19920902	EP 1991-918510	19910910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05503107	T2	19930527	JP 1991-517858	19910910

PRIORITY APPLN. INFO.: US 1990-581861 19900913
WO 1991-US6531 19910910

OTHER SOURCE(S): MARPAT 117:85989
GI



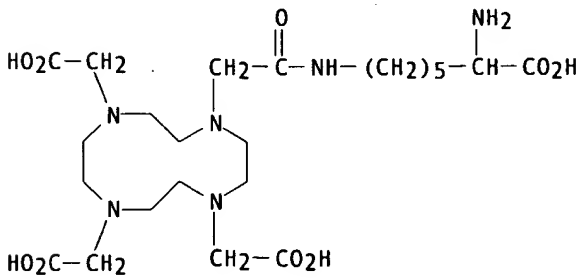
I

AB MRI imaging agents comprising a zwitterionic complex of a paramagnetic ion having a cyclic or open chain structure are prepd. Aminopentyl-EDTA [H2N(CH2)5CH[N(CH2CO2H)2CH2N(CH2CO2H)2] was prepd. and complexed with Gd. [[(7-Aminoheptyl)imino]bisethylenenitrilo]]tetraacetic acid and I were also prepd. as ligands.

IT **142958-12-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as ligand for MRI imaging complexes)

RN 142958-12-1 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-amino-6-carboxyhexyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 73 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:142782 CAPLUS
DOCUMENT NUMBER: 116:142782
TITLE: Multi-site metal chelating agents
INVENTOR(S): Love, David; Dow, William C.; Himmelsbach, Richard J.; Watson, Alan D.; Rocklage, Scott M.
PATENT ASSIGNEE(S): Cockbain, Julian Roderick Michaelson, UK; Salutar, Inc.
SOURCE: PCT Int. Appl., 96 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9105762	A1	19910502	WO 1990-EP1792	19901020
W: AU, CA, FI, HU, JP, NO, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5281704	A	19940125	US 1990-468107	19900119
AU 9066396	A1	19910516	AU 1990-66396	19901020
AU 647424	B2	19940324		
EP 497926	A1	19920812	EP 1991-908157	19901020
EP 497926	B1	19980603		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 62905	A2	19930628	HU 1992-1363	19901020
JP 05504125	T2	19930701	JP 1990-515144	19901020
AT 166864	E	19980615	AT 1991-908157	19901020
ES 2116291	T3	19980716	ES 1991-908157	19901020
JP 2000136174	A2	20000516	JP 1999-192219	19901020
FI 9201805	A	19920423	FI 1992-1805	19920423
NO 9201582	A	19920623	NO 1992-1582	19920423
AU 9453145	A1	19940317	AU 1994-53145	19940113
AU 656689	B2	19950209		

PRIORITY APPLN. INFO.:		GB 1989-23843	19891023
		GB 1990-1247	19900119
		US 1990-468107	19900119
		JP 1990-515144	19901020
		WO 1990-EP1792	19901020

AB There are disclosed polychelant compds., that is multi-site metal chelating agents, and chelates formed therewith. The polychelants and esp. their paramagnetic metal, heavy metal, or radioactive metal polychelates are particularly suitable for use in diagnostic imaging, heavy metal detoxification, or radiotherapy. The polychelants have a linear or branched oligomeric structure comprising alternating chelant and linker moieties bound together by amide or ester moieties, the carbonyl groups whereof being adjacent to the chelant moieties, each polychelant comprising .gtoreq.2 said chelant moieties capable of complexing a metal ion.

IT 137097-99-5
RL: RCT (Reactant)
(chelating agent, polychelant)

RN 137097-99-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10,10'-[1,2-ethanediylbis[imino(2-oxo-2,1-ethanediyl)]]bis- (9CI) (CA INDEX NAME)

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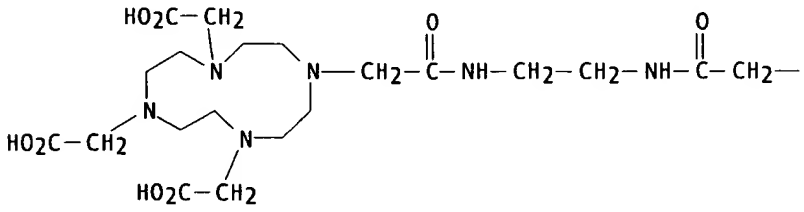
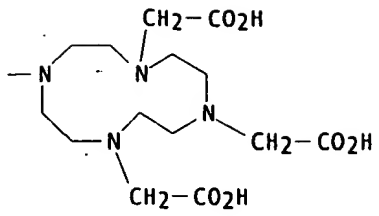
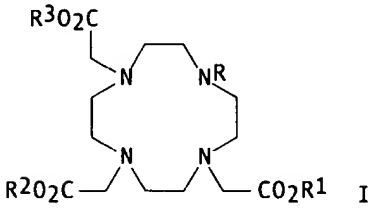




L10 ANSWER 74 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:21084 CAPLUS
DOCUMENT NUMBER: 116:21084
TITLE: Preparation of 1,4,7,10-tetraazacyclododecane-butyltriols and chelates as diagnostic and therapeutic agents
INVENTOR(S): Platzek, Johannes; Gries, Heinz; Weinmann, Hanns Joachim; Schuhmann-Giampieri, Gabriele D.; Press, Wolf-ruediger
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 448191	A1	19910925	EP 1991-250081	19910318
EP 448191	B1	19950628		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4009119	A1	19910926	DE 1990-4009119	19900319
NO 9101063	A	19910920	NO 1991-1063	19910318
NO 179610	B	19960805		
NO 179610	C	19961113		
CA 2038493	AA	19910920	CA 1991-2038493	19910318
HU 60478	A2	19920928	HU 1991-874	19910318
HU 215964	B	19990329		
JP 05320146	A2	19931203	JP 1991-77058	19910318
JP 2968367	B2	19991025		
ES 2074219	T3	19950901	ES 1991-250081	19910318
AU 9173610	A1	19910919	AU 1991-73610	19910319
AU 647091	B2	19940317		
FI 9101330	A	19910920	FI 1991-1330	19910319
IL 97592	A1	19951031	IL 1991-97592	19910319
PRIORITY APPLN. INFO.:			DE 1990-4009119	19900319

OTHER SOURCE(S): MARPAT 116:21084
GI



I

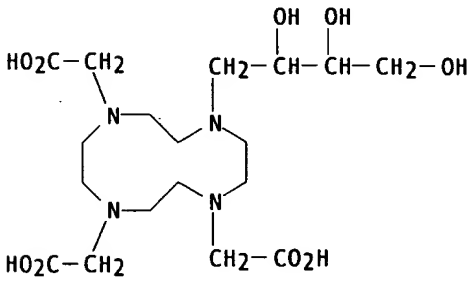
AB Title compds. (I; R = butyltriol residue; R1, R2, R3 = H, metal), were prepd. Thus, 4,7,10-tris(p-toluenesulfonyl)-1,4,7,10-tetraazacyclododecane and 4,4-dimethyl-3,5,8-trioxabicyclo[5.1.0]octane were treated in DMF at 170.degree. in an autoclave for 24 h to give 86% 10-(6-hydroxy-2,2-dimethyl-1,3-dioxepan-5-yl)-1,4,7-tris(p-

toluenesulfonyl)-1,4,7,10-tetraazcyclododecane. The latter was treated with Li in liq. NH3/THF and then with BrCH2CO2H/aq. KOH to give 10-(1-hydroxymethyl-1,2,3-dihydroxypropyl)-1,4,7-triscarboxymethyl-1,4,7,10-tetraazacyclododecane. The Gd complex of the latter was prepd. and used for NMR imaging of brain infarcts in rats.

IT 138147-53-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as chelating agent)

RN 138147-53-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3,4-trihydroxybutyl)- (9CI) (CA INDEX NAME)



L10 ANSWER 75 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:608034 CAPLUS

DOCUMENT NUMBER: 115:208034

TITLE: Preparation of 10-(2-hydroxy-3-alkoxypropyl)-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecanes as metal chelating agents, useful as contrast agents

INVENTOR(S): Dischino, Douglas D.

PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA

SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

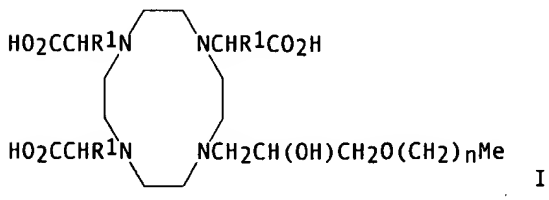
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 434345	A1	19910626	EP 1990-313790	19901217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 9067043	A1	19910627	AU 1990-67043	19901128
AU 625529	B2	19920716		
ZA 9009710	A	19911030	ZA 1990-9710	19901203
CA 2031585	AA	19910623	CA 1990-2031585	19901205
JP 04120065	A2	19920421	JP 1990-413421	19901221
HU 59115	A2	19920428	HU 1990-8437	19901221
PRIORITY APPLN. INFO.:			US 1989-454883	19891222

OTHER SOURCE(S): MARPAT 115:208034

GI



I

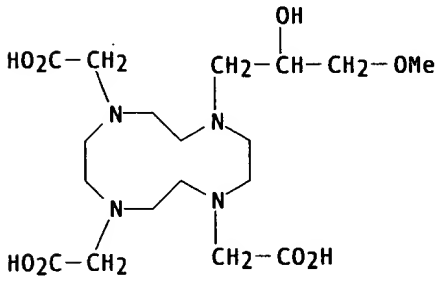
AB Title compds. I (R1 = H, alkyl; n = 0-5) and the gadolinium complex, useful as contrast agents (no data) are prepd. 1,4,7-Tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane was added to aq. NaOH, followed by glycidyl

Me ether to give after workup I (R1 = H, n = 0) (II). II in H2O was reacted with Gd2O3 at 90.degree. for 20.degree. to give the cyclodecanatogadolinium.

IT 136687-96-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as metal chelating agent)

RN 136687-96-2 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2-hydroxy-3-methoxypropyl)- (9CI) (CA INDEX NAME)



L10 ANSWER 76 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:608033 CAPLUS

DOCUMENT NUMBER: 115:208033

TITLE: Preparation of 10-(2-hydroxy-3-polyoxaalkylpropyl)-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane metal chelating ligand, useful as contrast agents

INVENTOR(S): Dischino, Douglas D.; Emswiler, John

PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA

SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

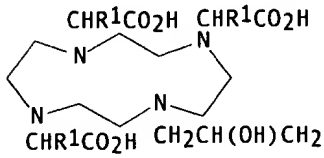
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 434346	A1	19910626	EP 1990-313791	19901217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 9067093	A1	19910627	AU 1990-67093	19901129
CA 2031587	AA	19910623	CA 1990-2031587	19901205
ZA 9009855	A	19911030	ZA 1990-9855	19901207
JP 04120066	A2	19920421	JP 1990-413422	19901221
HU 59114	A2	19920428	HU 1990-8436	19901221

PRIORITY APPLN. INFO.: US 1989-454890 19891222

OTHER SOURCE(S): MARPAT 115:208033

GI



I

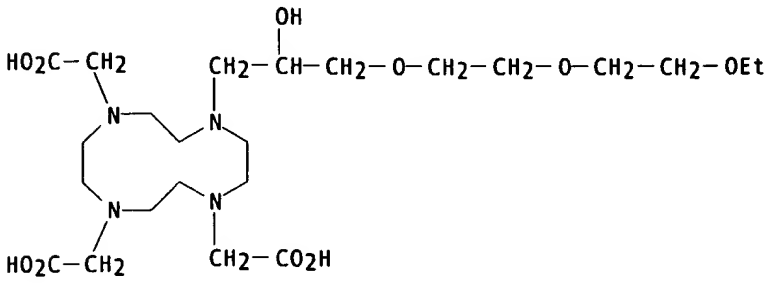
AB Title compds. I (R1 = H, alkyl; n, t = 2-5; r = 1-5; s = 0-5; p = 0, 1) useful as contrast agents (no data) are prepd. NaH in dry THF under N was added to EtOCH2CH2OCH2CH2OH followed by epichlorohydrin to give 1,2-epoxy-4,7,10-trioxadodecane which was treated with 1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane to give I (R1 = H, n = t = 2, r = s = p = 1) (II). To a soln. of II of pH 3.4 was added

Gd2O3 to give 1,4,7-tris(carboxymethyl)-10-(2-hydroxy-4,7,10-trioxadodecyl)-1,4,7,10-tetraazacyclododecanatogadolinium.

IT 136687-97-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as metal chelating ligand)

RN 136687-97-3 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[3-[2-(2-ethoxyethoxy)ethoxy]-2-hydroxypropyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 77 OF 83 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:420829 CAPLUS

DOCUMENT NUMBER: 115:20829

TITLE: Structure and solution stability of indium and gallium complexes of 1,4,7-triazacyclononanetriacetate and of yttrium complexes of 1,4,7,10-tetraazacyclododecanetetraacetate and related ligands: kinetically stable complexes for use in imaging and radioimmunotherapy. X-ray molecular structure of the indium and gallium complexes of 1,4,7-triazacyclononane-1,4,7-triacetic acid

AUTHOR(S): Broan, Christopher; Cox, Jonathan P.; Craig, Andrew S.; Kataky, Ritu; Parker, David; Harrison, Alice; Randall, Amanda M.; Ferguson, George

CORPORATE SOURCE: Dep. Chem., Univ. Durham, Durham, DH1 3LE, UK

SOURCE: J. Chem. Soc., Perkin Trans. 2 (1991), (1), 87-99
CODEN: JCPKBH; ISSN: 0300-9580

DOCUMENT TYPE: Journal

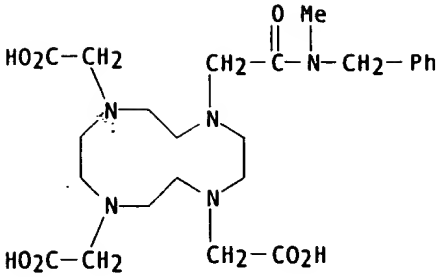
LANGUAGE: English

AB Of the 4 triazacycloalkanetriacetic acids screened for their ability to bind 111In, triazacyclononanetriacetate bound In most quickly and formed a complex whose dissocn. as a function of pD was monitored by 13C NMR spectrometry using a labeled ligand (k296 1.8 .times. 10-4 L mol-1 s0-1) pD 0 to -0.6. The corresponding Ga complex is even more stable with respect to acid dissocn. and may be obsd. by 71Ga NMR spectrometry both in vitro (.delta.Ga + 171 ppm) and in vivo. Crystal structures of the neutral Ga and of the protonated In (monoclinic, Z = 4) complexes are reported. The syntheses of a series of octadentate ligands are described and their relative efficiency to bind 90Y is reported. Ligands based on tetraazacyclododecane bind 90Y most rapidly, and tetraazacyclododecanetetraacetate forms a strong complex with Y (log K 24.9, 298 K) which dissocs. at low pH (<2) as measured by HPLC and 13C NMR spectrometry.

IT 132930-10-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 132930-10-0 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[methyl(phenylmethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

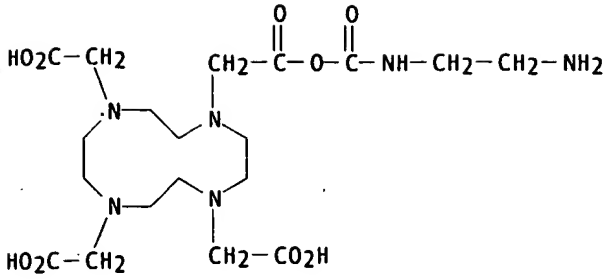


L10 ANSWER 78 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:415665 CAPLUS
DOCUMENT NUMBER: 115:15665
TITLE: Metal polychelates for conjugation to site-directed biomacromolecules for diagnostic imaging and rediotherapy
INVENTOR(S): Sieving, Paul F.; Watson, Alan D.; Quay, Steven C.; Rocklage, Scott M.
PATENT ASSIGNEE(S): Cockbain, Julian Roderick Michaelson, UK; Salutar, Inc.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9012050	A1	19901018	WO 1990-EP565	19900405
W: AU, CA, FI, HU, JP, NO, SU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5364613	A	19941115	US 1990-464865	19900116
AU 9054235	A1	19901105	AU 1990-54235	19900405
AU 656304	B2	19950202		
EP 474642	A1	19920318	EP 1990-906169	19900405
EP 474642	B1	19960626		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04504436	T2	19920806	JP 1990-505940	19900405
NO 9103920	A	19911127	NO 1991-3920	19911004
NO 178866	B	19960311		
NO 178866	C	19960619		
PRIORITY APPLN. INFO.:			US 1989-335162	19890407
			US 1990-464865	19900116
			WO 1990-EP565	19900405

AB Polychelants and their metal chelates are given which are useful in diagnostic imaging and in radiotherapy, and which comprise a plurality of macrocyclic chelant moieties, e.g. DOTA residues, conjugated to a polyamine backbone mol., e.g. polylysine. To produce a site-specific polychelate, one or more of the macrocyclic chelant carrying backbone mols. may be conjugated to a site-directed macromol., e.g. a protein. DOTA was reacted with iso-Bu chloroformate in tetramethylguanidine-contg. acetonitrile, to give DOTA carboxycarbonic anhydride, which upon treatment with mono-BOC-ethylenediamine yielded DOTA-N-(2-aminoethyl)amide. This was activated with thiophosgene, coupled with poly-L-lysine, and converted into a Gd complex. The Gd polychelate obtained was coupled to activated Igs for use in diagnosis.

IT 134314-87-7D, reaction product with polylysine
RL: BIOL (Biological study)
(polychelate, site-specific, for medicine)
RN 134314-87-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, monoanhydride with (2-aminoethyl)carbamic acid (9CI) (CA INDEX NAME)



IT 134314-84-4D, reaction product with polylysine
RL: BIOL (Biological study)
(polychelate, site-specific, for radiotherapy and radioimaging)
RN 134314-84-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, monoanhydride with [2-(4-aminophenyl)ethyl]carbamic acid (9CI) (CA INDEX NAME)

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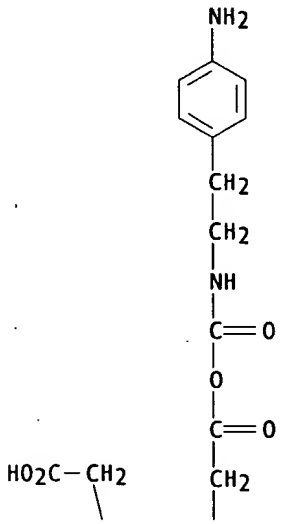
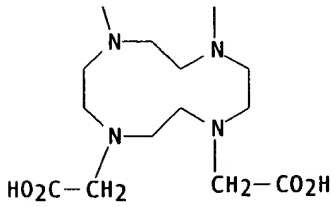
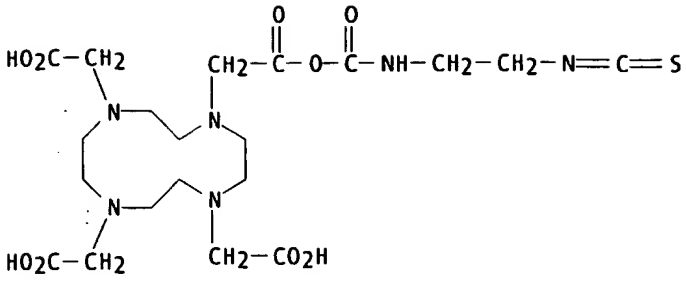


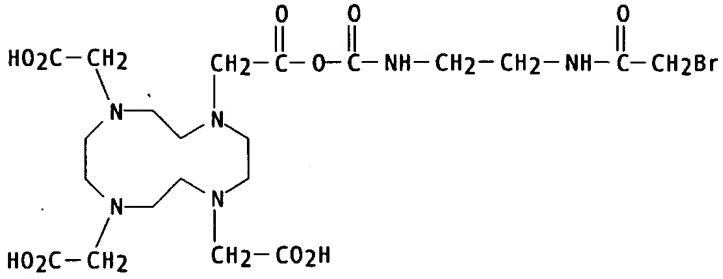
PAGE 2-A



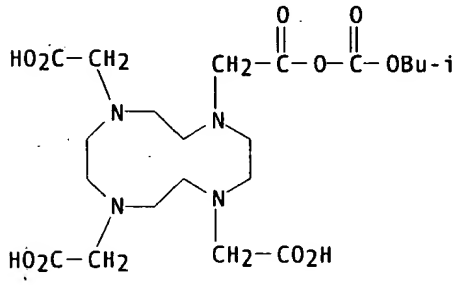
IT 134314-85-5P 134314-86-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with polylysine)
RN 134314-85-5 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, monoanhydride with (2-isothiocyanatoethyl)carbamic acid (9CI) (CA INDEX NAME)



RN 134314-86-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, monoanhydride with [2-[(bromoacetyl)amino]ethyl]carbamic acid (9CI) (CA INDEX NAME)



IT 124098-81-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with amines)
RN 124098-81-3 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, monoanhydride with 2-methylpropyl hydrogen carbonate (9CI) (CA INDEX NAME)

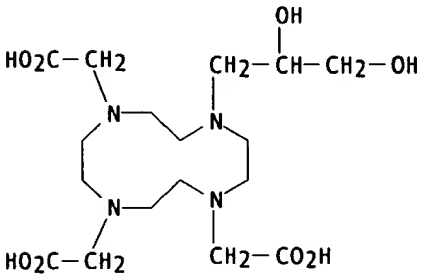


L10 ANSWER 79 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:177144 CAPLUS
DOCUMENT NUMBER: 114:177144
TITLE: Synthesis of nonionic gadolinium chelates useful as contrast agents for magnetic resonance imaging: 1,4,7-tris(carboxymethyl)-10-substituted-1,4,7,10-tetraazacyclododecanes and their corresponding gadolinium chelates
AUTHOR(S): Dischino, D. D.; Delaney, E. J.; Emswiler, J. E.; Gaughan, G. T.; Prasad, J. S.; Srivastava, S. K.; Tweedle, M. F.
CORPORATE SOURCE: Contrast Media Dep., Bristol-Myers Squibb Pharm. Res. Inst., New Brunswick, NJ, 08903-0191, USA
SOURCE: Inorg. Chem. (1991), 30(6), 1265-9
CODEN: INOCAJ; ISSN: 0020-1669
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of 1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane (I) was achieved through a variety of synthetic approaches. These routes

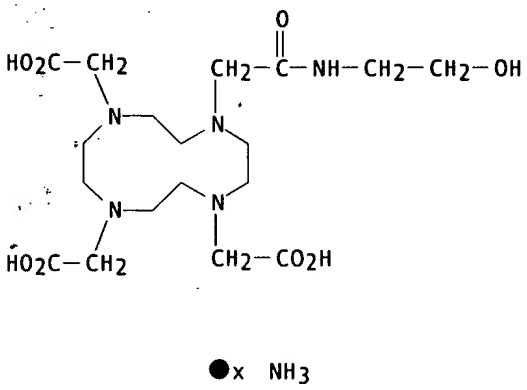
included (1) the partial carboxymethylation of unprotected 1,4,7,10-tetraazacyclododecane with CH2ClCO2H followed by ion-exchange chromatog., (2) reductive debenzylation (Pd/C, H2) of 1,4,7-(tris(carboxymethyl)-10-(phenylmethyl)-1,4,7,10-tetraazacyclododecane, and (3) carboxymethylation of 1-formyl-1,4,7,10-tetraazacyclododecane with CH2ClCO2H (or tert-Bu bromoacetate) followed by removal of the protecting group(s). The last method was the most efficient. The novel formyl cyclen was prepd. by the partial hydrolysis of 1,4,7,10-tetraazatricyclo[5.5.1.0]tridecane. I is versatile intermediate, being easily deriv. to produce potentially octadentate ligands and bifunctional chelating agents. A variety of octadentate ligands and their Gd(III) chelates were synthesized. Many of these Gd chelates are neutral, stable, and highly H2O sol. (>0.5 M), properties desirable in clin. useful magnetic resonance imaging contrast media.

IT **114873-42-6P 120041-18-1P 133008-72-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

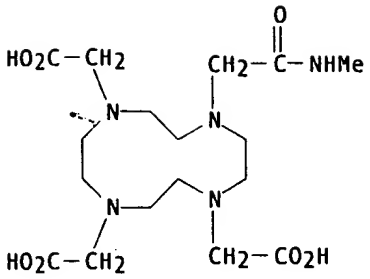
RN 114873-42-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3-dihydroxypropyl)- (9CI) (CA INDEX NAME)



RN 120041-18-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-hydroxyethyl)amino]-2-oxoethyl]-, ammonium salt (9CI) (CA INDEX NAME)



RN 133008-72-7 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-(methylamino)-2-oxoethyl]-, ammonium salt (9CI) (CA INDEX NAME)



●x NH_3

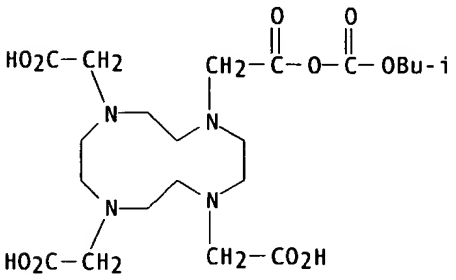
L10 ANSWER 80 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:94624 CAPLUS
DOCUMENT NUMBER: 112:94624
TITLE: Preparation and characterization of paramagnetic polychelates and their protein conjugates
AUTHOR(S): Sieving, Paul F.; Watson, Alan D.; Rocklage, Scott M.
CORPORATE SOURCE: Salutar, Inc., Sunnyvale, CA, 94086, USA
SOURCE: Bioconjugate Chem. (1990), 1(1), 65-71
CODEN: BCCHES
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Gd complexes of poly-L-lysine-poly(DTPA) (Gd-PL-DTPA) and poly-L-lysine-poly(1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid) (Gd-PL-DOTA) and their conjugates with human serum albumin (HSA) have been prepd. and characterized. Poly-L-lysine (PL, degree of polymn. .apprxeq. 100) was N-acylated with a mixed anhydride of the chelating ligand (DTPA or DOTA), and 60-90 chelating groups per mol. of PL could be attached in this way. Following purifn. of the polychelate by size-exclusion chromatog., the Gd complexes were prepd. by std. methods and conjugated to HSA with heterobifunctional crosslinking reagents. The molar relaxivities of these macromol. species were 2-3-fold higher than those of the corresponding monomeric metal complexes ([Gd(DTPA)] and [Gd(DOTA]). The conjugation conditions were optimized to produce conjugates contg. 60-90 metal centers per mol. of HSA (.apprx.1 polychelate per protein).

IT **124098-82-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conjugation to polylysine)
RN 124098-82-4 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid, monoanhydride with 2-methylpropyl hydrogen carbonate, compd. with N,N,N',N'-tetramethylguanidine (1:3) (9CI) (CA INDEX NAME)

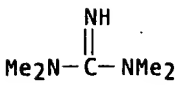
CM 1

CRN 124098-81-3
CMF C21 H36 N4 O10



CM 2

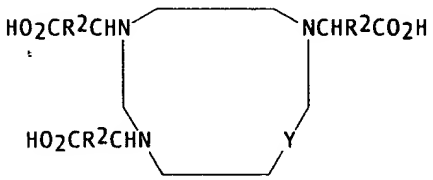
CRN 80-70-6
CMF C5 H13 N3



L10 ANSWER 81 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:173270 CAPLUS
DOCUMENT NUMBER: 110:173270
TITLE: Preparation of substituted 1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane and analogs as metal-chelating ligands useful in diagnostic medicine
INVENTOR(S): Tweedle, Michael F.; Gaughan, Glen T.; Hagan, James J.
PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 292689	A2	19881130	EP 1988-106139	19880418
EP 292689	A3	19910731		
EP 292689	B1	19960731		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4885363	A	19891205	US 1987-137267	19871223
CA 1296715	A1	19920303	CA 1988-562796	19880329
JP 01052764	A2	19890228	JP 1988-99263	19880421
PRIORITY APPLN. INFO.:			US 1987-42416	19870424
			US 1987-137267	19871223
			US 1986-821725	19860123

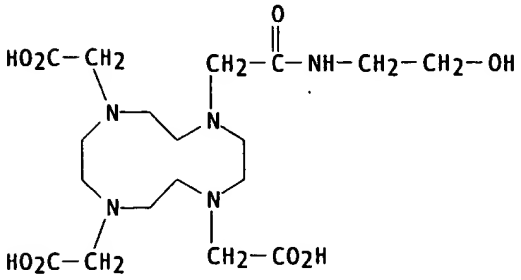
OTHER SOURCE(S): MARPAT 110:173270
GI



I

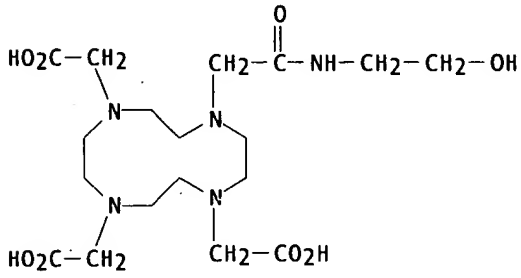
AB Title compds. [I; Y = O, R1N; R1 = H, C1-10 alkyl, aryl-C1-10 alkyl, aryl, C1-10 alkoxy, C1-10 hydroxyalkyl, 4-GC6H4CH2CH(NH2)CO(CH2)n, 4-GC6H4(CH2)n, G(CH2)n, etc.; G = amino, isothiocyanato, etc.; R2 = H, C1-10 alkyl; n = 0-5] and their salts, which are metal chelating ligands useful in diagnostic medicine (no data) are prepd. ClCH2CO2H was added to a soln. of 1-oxa-4,7,10-triazacyclododecane.H2SO4 in 6M KOH and the mixt. was heated 15 h at 45.degree. to give I (R2 = H; Y = O) (II). II was added to aq. Gd(OAc)3, the pH was adjusted to 3 and the mixt. heated at 88.degree. for 20 min, the pH was adjusted to 7.3, and the procedure repeated twice to give a Gd(III) chelate of II which was clear at pH 7.3. The chelate soln. was passed through a 0.22 .mu.m filter into a vial and sealed.
IT 120041-18-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decompn. and complexation of)
RN 120041-18-1 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-hydroxyethyl)amino]-2-oxoethyl]-, ammonium salt (9CI) (CA INDEX NAME)

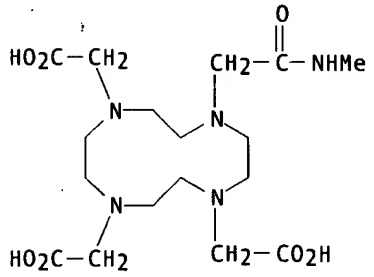


● x NH_3

IT 114873-48-2P 120041-07-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as ligand for diagnostic medicine)
RN 114873-48-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-hydroxyethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 120041-07-8 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-(methylamino)-2-oxoethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 82 OF 83 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:64610 CAPLUS
DOCUMENT NUMBER: 110:64610
TITLE: Synthesis and characterization of the gadolinium(3+) complex of DOTA-propylamide: a model DOTA-protein conjugate
AUTHOR(S): Sherry, A. Dean; Brown, Rodney D., III; Geraldes, Carlos F. G. C.; Koenig, Seymour H.; Kuan, Kah Tiong; Spiller, Marga
CORPORATE SOURCE: Dep. Chem., Univ. Texas Dallas, Richardson, TX, 75083-0688, USA

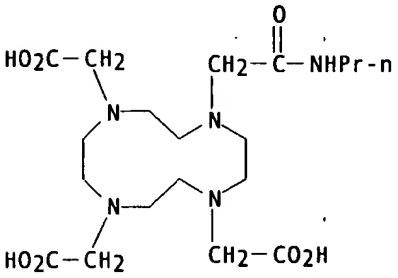
SOURCE: Inorg. Chem. (1989), 28(3), 620-2
CODEN: INOCAJ; ISSN: 0020-1669
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The monopropylamide deriv. (H3DOTA-PA) of 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (H3DOTA) was prepd. and characterized. Like the parent macrocycle DOTA, it forms a complex with Gd3+ only slowly at room temp. but with a 104.5 lower stability const. The frequency dependence of the solvent water proton spin-lattice relaxation rates for the 2 complexes indicates that both contain 1 water mol. in the primary coordination sphere of the Gd3+, but that the electron-spin correlation time, .tau.SO, is considerably shortened in the Gd(DOTA-PA) vs. the Gd(DOTA)- complex. The implications and advantages of attaching DOTA to a protein to provide magnetic resonance contrast vs. the more commonly used DTPA-conjugated systems is discussed.

IT **118476-80-5DP**, gadolinium complex
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, NMR imaging contrast agent in relation to)

RN 118476-80-5 CAPLUS

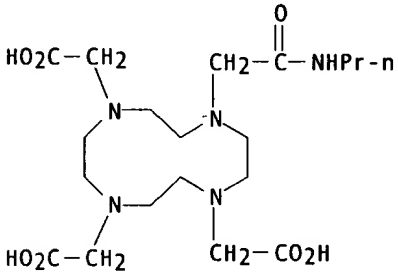
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-(propylamino)ethyl]- (9CI) (CA INDEX NAME)



IT **118476-80-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ionization of)

RN 118476-80-5 CAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-oxo-2-(propylamino)ethyl]- (9CI) (CA INDEX NAME)



L10 ANSWER 83 OF 83 CAPLUS COPYRIGHT 2001 ACS

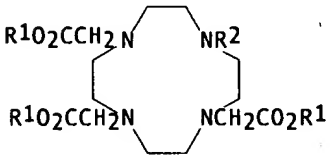
ACCESSION NUMBER: 1988:406552 CAPLUS
DOCUMENT NUMBER: 109:6552
TITLE: Preparation of 1,4,7,10-tetraazacyclododecane-1,4,7-triacetates and their metal salts and complexes as diagnostic aids for x-ray and tomographic diagnoses
INVENTOR(S): Gries, Heinz; Raduechel, Bernd; Speck, Ulrich; Weinmann, Hanns Joachim
PATENT ASSIGNEE(S): Schering A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3625417	A1	19880211	DE 1986-3625417	19860728
DE 3625417	C2	19981008		
EP 255471	A1	19880203	EP 1987-730085	19870724
EP 255471	B1	19920909		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 80391	E	19920915	AT 1987-730085	19870724
ES 2052599	T3	19940716	ES 1987-730085	19870724
NO 8703132	A	19880129	NO 1987-3132	19870727
NO 174048	B	19931129		
NO 174048	C	19940309		
AU 8776217	A1	19880204	AU 1987-76217	19870727
AU 604249	B2	19901213		
DK 8703933	A	19880129	DK 1987-3933	19870728
DK 171574	B1	19970120		
JP 63041468	A2	19880222	JP 1987-186794	19870728
JP 07053720	B4	19950607		
ZA 8705561	A	19890329	ZA 1987-5561	19870728

PRIORITY APPLN. INFO.: DE 1986-3625417 19860728
EP 1987-730085 19870724

OTHER SOURCE(S): MARPAT 109:6552
GI



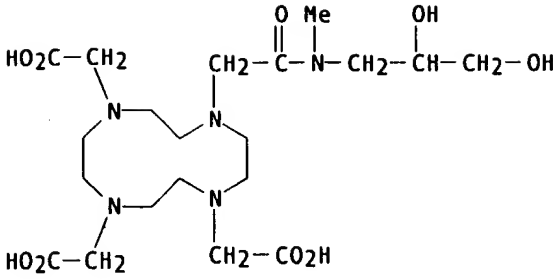
I

AB The title compds. [I; R1 = H, metal ion equiv.; R2 = H, B, BCOCH2, R3R4NZCH2, (un)satd. C1-10 alkyl, alkanoyl, optionally substituted by OH, alkoxy; B = biomol. residue; R3,R4 = H, C1-16 alkyl, optionally substituted by OH, alkoxy; R3R4N = 5- or 6-membered heterocyclyl; R2,R3 may represent a second tetraazacyclododecane moiety bound via an (un)substituted, difunctional acyl or hydrocarbon group; Z = CO, C1-10 alkylene, optionally interrupted with Oand having OH and alkoxy substituents], their salts, metal complexes, and conjugates with biomols., were prepd. as imaging aids for x-ray, scintigraphic, and tomog. diagnosis (no data). N, N',N''-Tris(p-tolylsulfonyl)diethylenetriamine di-Na salt and N,N-bis[(p-tolylsulfonyl)oxy]ethyl]benzylamine were heated at 100.degree. in DMF to give 1-benzyl-4,7,10-tris(p-tolylsulfonyl)-1,4,7,10-tetraazacyclododecane. This was detosylated by heating at 50.degree. in HBr/HOAc/PhOH and alkylated with BrCH2CO2Et to give I (R1 = Et, R2 = PhCH2). The latter was debenzylated by hydrogenation over Pd/C, and the resulting triester was sapond. with 3 N NaOH and, without isolation, treated with Gd(OAc)3 and stirred 3 h at 60.degree. to give the Gd(III) complex of I (R1 = R2 =H) (1:1).

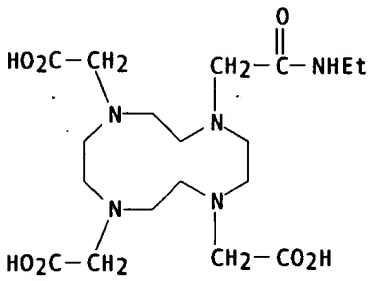
IT **114873-38-0P 114873-39-1P 114873-42-6P**
114873-48-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and complexation of, for tomog. and x-ray contrast agents)

RN 114873-38-0 CAPLUS

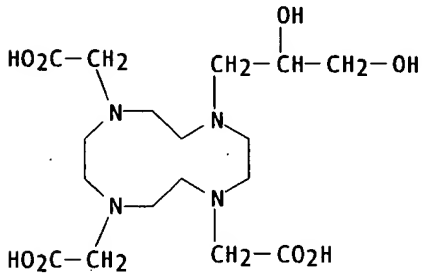
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2,3-dihydroxypropyl)methylamino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



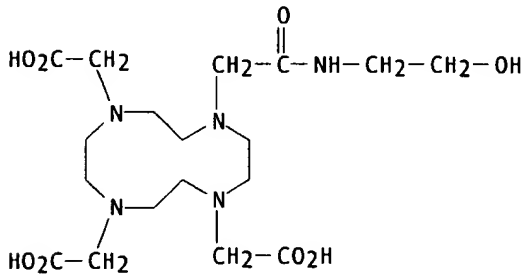
RN 114873-39-1 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-(ethylamino)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 114873-42-6 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-(2,3-dihydroxypropyl)- (9CI) (CA INDEX NAME)



RN 114873-48-2 CAPLUS
CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(2-hydroxyethyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



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US 0941602207P1

Creation date: 04-26-07
Indexing Officer: TBUI2 - THU-TRANG BUI
Team: ZZZFEP
Dossier: 09416022

Legal Date: 04-02-01

No.	Doccode	Number of pages
1	A...	1
2	CLM	4
3	REM	9

Total number of pages: 14

Remarks:

Order of re-scan issued on .....